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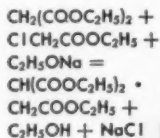
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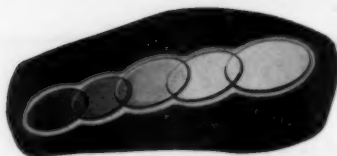
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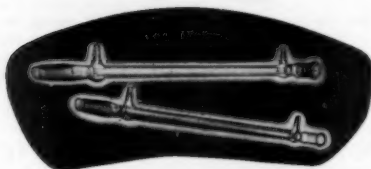
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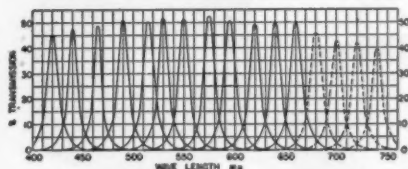
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Preparation of Graphs for Science

These suggestions are intended for the guidance of authors and draftsmen in preparing graphs for reproduction. They do not comprise a comprehensive set of suggestions but merely emphasize certain practices that often are disregarded. Although the discussion is confined to the simplest types of graph, many of the suggestions are applicable to line drawings in general. Most of the recommendations are in accord with those made in American Standards Association publication Z15.3.

Not more than three or four curves ordinarily should be shown on the same graph, although more may be included in the case of a family of well-separated curves. Use a solid line for an especially important curve and dashed, dotted, or lighter solid lines for the other curves. No curve or coordinate ruling of the graph should run through any lettering or outlined circles, triangles, and so forth, that are used to indicate plotted points.

Coordinate rulings should be limited in number to those needed to guide the eye in making a reading to the desired degree of approximation. Short scale markers, or "ticks," may be inserted between rulings if this is desirable. The rulings should be light enough not to distract attention from the curves being presented.

Lettering should be placed so as to be easily read from the bottom and from the right-hand side of the graph; that is, the lettering should face either the bottom or the right-hand side of the drawing.

A graph should be free of all lines and lettering that are not essential for clear understanding. As far as practicable, explanatory comments, supplementary data, or formulas should be placed in the figure legend or in the text. The exception to this rule is the case where there are several curves on the same graph that need separate identification; if practicable, they should be identified by brief labels placed close to the curve (horizontally or along the curve) rather than by single letters or numbers requiring a key.

If it seems necessary to place supplementary information on the drawing proper, the lettering should be kept within the vertical and horizontal limits of the curves or other essential features of the drawing. Otherwise the space occupied by the drawing may be needlessly large, or else the drawing may have to be reduced in reproduction, often to the point where the lettering or other details are illegible.

Scale captions should be placed outside the grid area, usually at the bottom toward the right for the horizontal scale and at the left-hand side toward the top for the vertical scale. The scale caption should consist of (i) the name of the variable plotted, (ii) its symbol, if one is used in the text, and (iii) in parentheses, the abbrevia-

tion for the unit of measure; thus, Pressure p (lb./in.²). Avoid using such captions as "Pressure in lb./in." and "Pressure in lb per sq in." The technical terms, symbols, and abbreviations on a drawing should be in accord with those used in the text of the article.

The horizontal and vertical scales for a graph should be chosen with care, so as to give a correct impression of the relationship plotted, for the choice of scales has a controlling influence on the apparent rate of change of the dependent variable. Except where a visual comparison of plotted magnitudes is important, the bottom (abscissa) and extreme left-hand (ordinate) coordinate lines need not represent the zero values of the variables plotted: this often results in a more effective graph as well as a saving of space.

The numerals representing the scale values should be placed outside the grid area. If the scale values are smaller than unity and are expressed in decimal form, a cipher should always precede the decimal point; thus, 0.20, not .20.

The use of many ciphers in scale numbers should be avoided, and the best way to do this is to reexpress the quantity plotted in terms of a larger unit of measurement. For example, suppose that originally the scale numbers are 15 000, 20 000, 25 000 . . . and that the scale caption is "Pressure (lb./in.²)"; these scale numbers can be changed to 15, 20, 25, . . . , provided that the unit is changed to 10³ lb./in.². If, in this example, the data are correct to three significant figures and it is desirable to indicate this fact, then the scale figures should be 1.50, 2.00, 2.50, . . . , and the unit, 10³ lb./in.². Never use captions of the types: "Velocity $\times 10^3$ in ft/sec" and "Velocity (ft/sec $\times 10^3$). They are ambiguous, since they do not indicate clearly whether the scale numbers have been or are to be multiplied by 10³.

A brief legend should be provided for each graph. All legends are set in type and hence should be typewritten double-spaced, in a list on a separate page.

Black drawing ink should be used. Many writing inks do not reproduce well. Drawings should be made on tracing cloth, tracing paper, or a fairly heavy white paper having a dull surface that will stand erasure without roughening. Ruled coordinate paper may be used, provided that it is printed in light blue; the important coordinate lines and scale markers that are intended to appear in the reproduction must be ruled in ink.

A good size for a drawing is double that desired for the printed figure; all lettering and line thicknesses should be increased accordingly. Thus, a drawing that is to be reproduced column-width in *Science* should be made not more than 6 in. wide over-all. A simple drawing containing little detail may often be so planned that the printed figure can be made less than column-width.—D. R.

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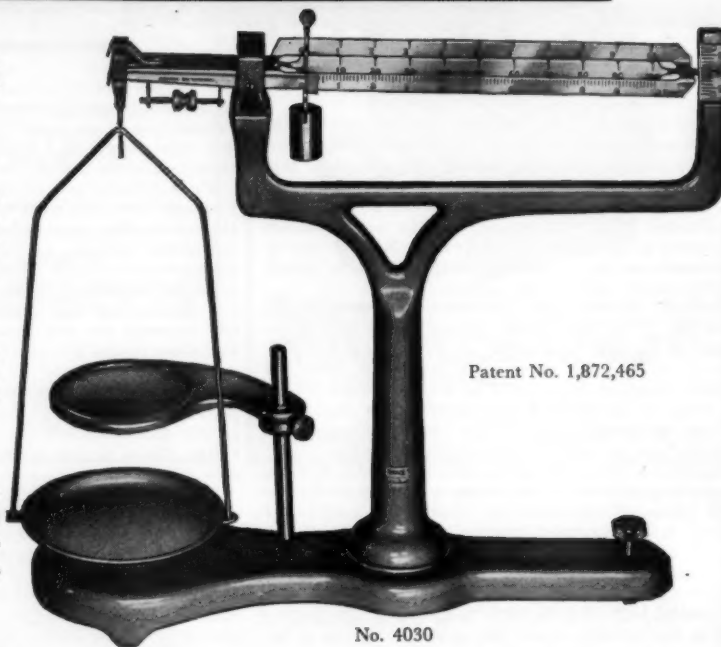
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Significance of Enzymatically Catalyzed Exchange Reactions in Chemotherapy

Nathan O. Kaplan, Abraham Goldin, Stewart R. Humphreys,
Margaret M. Ciotti, John M. Venditti

McCullum-Pratt Institute, The Johns Hopkins University, Baltimore, and
Laboratory of Chemical Pharmacology, National Cancer Institute,
National Institutes of Health, U.S. Public Health Service, Bethesda, Maryland

IT has been previously reported that animal tissue DPNases can catalyze an exchange reaction between the nicotinamide moiety of DPN and compounds related to nicotinamide according to the equation (1)



The pyridine compounds that to date have been found to undergo exchange with nicotinamide are isonicotinamide (2), isonicotinic acid hydrazide (2-4), marsilid (the isopropyl derivative of isonicotinic acid hydrazide) (2), 3-acetyl pyridine (5) and ethyl nicotinate (6); the resulting corresponding DPN analogs have now all been isolated.

The fact that analogs of DPN can be formed by an exchange reaction *in vitro* suggests the possibility that antimetabolites of nicotinamide might exert their pharmacologic action through such a mechanism. Furthermore, if these reactions occur in the whole animal, they may be of significance in developing a new type of approach for the use of chemotherapeutic agents. This paper (7) is the result of a preliminary effort to make use of an understanding of enzymatic mechanisms toward the development of pharmacologically active compounds. Evidence is presented that exchange reactions occur *in vivo*. In addition, this report is concerned with the significance of enzymatically catalyzed exchange reactions in elucidating the toxic action of an antimetabolite such as 3-acetyl pyridine.

Woolley (8) has found that feeding 3-acetyl pyridine to mice will produce symptoms of nicotinic acid deficiency when the level of the vitamin in the diet is low. Addition of either nicotinic acid or nicotinamide to the diet relieved the animals from the symptoms induced by the acetyl pyridine. Table 1 summarizes the toxicity studies that we have carried out on mice. Intraperitoneal administration of 500 mg of compound per kilogram of body weight usually results in 100 percent mortality. Most of the deaths occur about 4 hr after the injection of acetyl pyridine. The primary signs of toxicity seem to result from disturbance of the central nervous system. Details of the toxic manifestations will be presented elsewhere (9).

Table 1 also shows that the simultaneous administration of nicotinamide from 250 to 1000 mg/kg affords marked protection against the lethal effects of acetyl pyridine. It is of interest to note also that admin-

istered DPN has a protective action. In contrast, nicotinic acid does not protect against toxicity. Tryptophan also appears to be without effect (10, 11).

The fact that nicotinamide can protect the animals against the toxicity of the antimetabolite, whereas the acid does not, is of considerable interest, particularly since nicotinic acid and nicotinamide are considered to be of equal value in the diet. The inability of nicotinic acid to protect appears to be related to the finding that tissue DPNases do not promote an exchange between the nicotinamide of DPN and free nicotinic acid. On the other hand, it has been found by the use of C¹⁴-labeled nicotinamide that animal DPNases will catalyze an exchange between the bound nicotinamide and free nicotinamide (12). In Table 2, data are presented that show that nicotinamide inhibits the formation of the acetyl pyridine analog from DPN and acetyl pyridine in a mouse brain homogenate. Nicotinic acid, in contrast, has no such effect.

From the results given in Tables 1 and 2, it appears likely that the toxicity rendered by the injection

Table 1. Effect of metabolites on the lethal toxicity of 3-acetyl pyridine in mice.*

Metabolite	Dose (mg/kg)	3-Acetyl pyridine (500 mg/kg)
		Dead/total
Nicotinamide	1000	0/12
	500	0/12
	250	0/12
DPN	1500	0/6
	1000	0/12
	500	1/12
	250	2/6
Nicotinic acid	1000	6/6
	500	6/6
	250	6/6
Tryptophan (pt.)	1000	5/6
	500	6/6
	250	6/6
Controls	No metabolite	23/23

* Metabolite administered intraperitoneally immediately prior to the administration of 3-acetyl pyridine subcutaneously. Mice: C x DBA hybrid ♂ 8 to 10 wk old.

of 3-acetyl pyridine is related to the formation of the corresponding analog of DPN. The protection produced by nicotinamide *in vivo* is certainly closely correlated to the inhibition of synthesis of the analog *in vitro*. Although nicotinamide and nicotinic acid are interchangeable in the diet, these compounds are not interchangeable in combatting antimetabolites such as 3-acetyl pyridine. The ineffectiveness of nicotinic acid *in vivo* indicates that exchange reactions do occur *in vivo*, since if a synthetic system was involved it might be expected that the acid would protect because it can replace nicotinamide in the diet. It therefore seems of importance in studying the action of an antimetabolite to ascertain whether the antimetabolite acts by competing with the metabolite in a synthetic reaction (that is, the synthesis of DPN from nicotinamide) or in exchange reactions of the DPNase type.

Table 2 demonstrates that nicotinamide has a somewhat greater affinity for the mouse brain DPNase than does the 3-acetyl pyridine. This is manifested in the inhibition of analog synthesis by the use of a considerably lower nicotinamide level. A concentration of 0.01M nicotinamide is effective in inhibiting the analog formation 69 percent in the presence of 0.1M acetyl pyridine. Figure 1 shows the effect of nicotinamide on the median lethal dose (LD_{50}) of acetyl pyridine (13, 14). It may be observed that by increasing the amount of nicotinamide injected, a pronounced increase in the LD_{50} takes place. The protective effect of nicotinamide reaches a maximum at a level of 250 to 500 mg/kg of body weight. Further increase in nicotinamide concentration results in a loss in protection against the toxicity of the acetyl pyridine. This deleterious effect of excess nicotinamide is apparently due to the nicotinamide itself, since the metabolite itself produces toxicity when administered at a level of 2000 mg/kg or more.

Nicotinamide, when administered up to a period of

Table 2. Effect of nicotinamide and nicotinic acid on acetyl pyridine analog formation in mouse brain. Reaction mixtures contained 0.32 micromoles DPN, 0.1 ml mouse brain homogenate, 0.1M 3-acetyl pyridine, 0.05M phosphate (pH 7.5), total volume 0.6 ml, temp. 37°C, incubation time, 35 min.

Metabolite (mole)	3-Acetyl pyridine analog of DPN formed* (μ mole)	Inhibition of analog formation (%)
Nicotinamide		
0.0	0.202	
.2	.0	100
.1	.014	93
.05	.034	83
.01	.063	69
.001	.180	10
Nicotinic acid		
0.1	0.192	4
.01	.210	0

* Analog determined by change in optical density at 400 m μ after addition of yeast alcohol dehydrogenase (6).

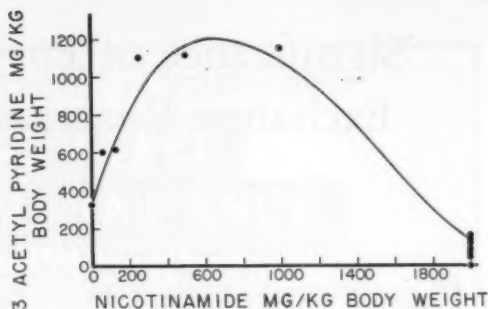


Fig. 1. Effect of nicotinamide on the median lethal dose (LD_{50}) of acetyl pyridine in mice.

2 to 3 hr after a lethal dose of acetyl pyridine is given, still has a protective influence. When the vitamin is given 4 hr prior to the antimetabolite, protection is again observed. If the nicotinamide, however, is administered more than 4 hr before the acetyl pyridine is introduced, a decrease in protection results. The fact that acetyl pyridine acts very rapidly, together with the characteristics of the antagonistic properties of nicotinamide, is certainly indicative that the lethal action of the compound is due to the exchange reaction catalyzed by the DPNase. Complete results of the time relationships of nicotinamide protection will be published elsewhere (9).

The dose-mortality response curve of 3-acetyl pyridine in mice is shown in Fig. 2. The $LD_{50} \pm 1$ S.E. is 305.5 ± 12.5 mg/kg. The slope of the line is 12.51 prohibits per tenfold increase in dose. Many deaths from acute toxicity occurred from 4 to 24 hr following administration of the antimetabolite. Additional deaths occurred as late as 6 days following drug administration. The animals in the latter group showed evidence of chronic toxicity, including anorexia and weight loss. Although it did not occur here, in other experiments treated animals occasionally did not succumb until 10 to 20 days following administration of the antimetabolite. At toxic levels of the antimetabolite, survivors of drug mortality showed evidence of anorexia and loss of weight. Acute toxicity occurs primarily at high doses of the drug. Chronic toxicity becomes more evident at doses just below the level of acute toxicity. The toxicity of acetyl pyridine when administered with nicotinamide is dependent upon the relative doses of antimetabolite and metabolite employed. Administration of appropriate doses of nicotinamide protects against both acute and chronic toxicity of acetyl pyridine.

The curve in Fig. 2 is quite steep. In fact, it appears to be twice as steep as similar plots obtained with 6-mercaptopurine or aminopterin (15). It is of interest to examine the significance of the curve particularly with respect to the fate of administered acetyl pyridine. It is known that acetyl pyridine can partially fulfill the nicotinamide or nicotinic acid requirement in the diet (16). It has also been found that administration of acetyl pyridine to animals re-

sults in the presence of nicotinamide and N-methyl nicotinamide in the urine (17-19). It thus appears likely that acetyl pyridine can be converted to either nicotinic acid or to its amide.

Further evidence confirming the conversion of acetyl pyridine to nicotinamide is presented in Table 3. Injection of acetyl pyridine to mice leads to a four-fold rise in the DPN level of the liver. Nicotinamide produces an eightfold increase in the liver coenzyme content. This exceptionally great increase in pyridine nucleotide content was quite unexpected (20). It is of interest to note that we have found that acetyl pyridine is a better precursor of DPN in the liver than nicotinic acid is. The mechanism by which acetyl pyridine is converted to nicotinamide bound in DPN is now under investigation in this laboratory.

Although acetyl pyridine does give rise to DPN, no acetyl pyridine analog was found in the liver. Hence it appears that the liver converts acetyl pyridine to nicotinamide and that a large amount of acetyl pyridine would be detoxified by such a conversion. However, the conversion of acetyl pyridine to free nicotinamide or nicotinamide bound in DPN does not occur in a number of other tissues. An investigation of extrahepatic tissues indicated that some analog was formed in the brain and in the spleen after injection of the acetyl pyridine. No increase in DPN occurred in these tissues after the introduction of the antimetabolite.

One explanation of the steepness of the curve in Fig. 2 might be that acetyl pyridine can be handled by the liver up to a certain amount, but after the liver becomes saturated with the compound the excess might then become incorporated as analog via the DPNase system in the extrahepatic tissues. The toxicity of acetyl pyridine may therefore be due to formation of the analog in the nervous system.

Acetyl pyridine is in a sense unique in that it is an

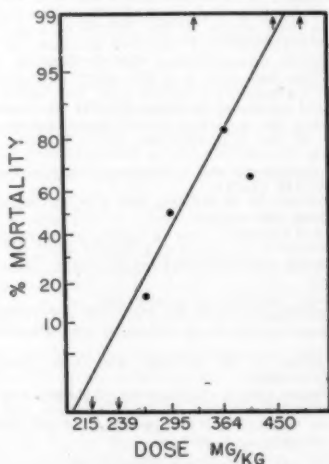


Fig. 2. Dose-mortality response curve of 3-acetyl pyridine in mice. 0 percent or 100 percent mortality represented by arrows.

Table 3. Effect of acetyl pyridine and nicotinamide injection on DPN* content of mouse liver. Animals were sacrificed 3 to 3½ hr after intraperitoneal administration of various substances. All values are in micrograms per gram of fresh liver.

Animal	Control†	Acetyl pyridine injected‡	Nicotinamide injected§
1	450	1690	2840
2	408	1850	3420
3	482	1400	3140
4	350	1750	3050
Average	423	1690	3165

* Represents both DPN and TPN concentrations.

† Injected with 0.85 percent saline.

‡ Given 500 mg of acetyl pyridine per kilogram of body weight.

§ Given 500 mg of nicotinamide per kilogram of body weight.

antimetabolite that can be detoxified by its conversion to the metabolite. The compound is also of interest from a pharmacologic point of view, because its toxicity depends greatly on the differences in its reactivity in various tissues.

As mentioned in a preceding paragraph, the acetyl pyridine analog of DPN was detected in both brain and spleen (21). The highest concentration of analog after the injection of acetyl pyridine was found in neoplastic tissues. Three different strains of tumors (Leukemia L1210, Bashford Carcinoma, and Sarcoma 37) all yielded relatively large amounts of the analog after administration of the antimetabolite. Table 4 gives representative data with the leukemia. Nicotinamide injection produced some increase in the DPN content of the leukemia. Acetyl pyridine administration, in contrast to the picture in liver, caused a decrease in the DPN level of the tumor. The decrease in DPN can be largely accounted for by synthesis of the analog (Table 4). When nicotinamide was given with the acetyl pyridine, a significant decrease in the amount of the analog occurred. Results similar to those in Table 4 were obtained with both Sarcoma 37 and Bashford Carcinoma.

The analog has been isolated from the leukemia by precipitation with acetone after removal of proteins with trichloroacetic acid. The DPN present was cleaved with Neurospora DPNase (22), which does not split the acetyl pyridine analog (5). The acetyl pyridine analog was identified by its reduced spectrum (maximum at 365 mμ) after reaction with yeast alcohol dehydrogenase and alcohol (5).

Whether the toxic effects of acetyl pyridine are manifested in the analog itself or are caused by a decrease in the DPN level resulting from formation of the analog is not yet clear. Attempts to clarify this point have been undertaken by injection of the 3-acetyl pyridine analog of DPN itself. Preliminary experiments indicate that the DPN analog is not as toxic as free acetyl pyridine. Work is now also in progress on the activities of acetyl pyridine and the acetyl pyridine analog in tumor therapy.

It is our view that the demonstration of the forma-

Table 4. Effect of acetyl pyridine and nicotinamide injection on the pyridine nucleotide content of mouse leukemia. Animals were given various intraperitoneal injections and were sacrificed 3 hr after injection. All values are in micrograms per gram of fresh tissue.

Animal	Control*	Nicotinamide†	Acetyl pyridine‡		Acetyl pyridine and nicotinamide§	
	DPN	DPN	DPN	Analog	DPN	Analog
1	141	360	87	49	311	19
2	131	321	102	49	145	11
3	150	326	102	44	204	19
4	150	282	55	33		
5	136	282	93	49		
Average	141	322	86	42	220	17

* Injected with saline.

† Injected with 1000 mg nicotinamide per kilogram of body weight.

‡ Injected with 1000 mg acetyl pyridine per kilogram of body weight.

§ Injected with both 1000 mg nicotinamide and 1000 mg acetyl pyridine per kilogram of body weight.

tion of a coenzyme analog in the intact animal is of importance in elucidating a system of chemotherapy. Coenzymes are the functional forms of the vitamins and, as such, they occupy key positions in metabolism. A decrease in effective concentration by the formation of analogs would be expected to interfere with the normal functions of cells. This is illustrated by the metabolic disturbances that are associated with vitamin deficiency. Exchange reactions that involve coenzymes appear to be a rapid means of producing coenzyme analogs *in vivo* and, as a result, a rapid means for inhibiting or altering cellular metabolism. This is illustrated by the marked acute toxicity of such a compound as acetyl pyridine. An appreciation of the antimetabolite-metabolite relationship as applied to enzymes catalyzing exchange reactions is highly desirable, and it is to be hoped that further work on this problem not only will be of value from the viewpoint of chemotherapy but also will aid us to understand the significance of enzymatically catalyzed exchange reactions.

SUMMARY

1) 3-Acetyl pyridine has been found to be quite toxic when administered to mice. Simultaneous administration of nicotinamide or DPN protects against the toxicity of acetyl pyridine. Nicotinic acid and tryptophan do not protect animals from the lethal effects of the compound.

2) Nicotinamide inhibits the formation of the 3-acetyl pyridine analog of DPN from acetyl pyridine and DPN in mouse brain homogenates. Nicotinic acid has no inhibitory effect on analog synthesis.

3) Administration of acetyl pyridine results in a fourfold increase in the DPN level of the liver. No acetyl pyridine analog of DPN is found in the liver after injection of the antimetabolite.

4) Injection of acetyl pyridine into tumor mice results in the formation of the acetyl pyridine analog of DPN in the neoplastic tissues. A decrease in DPN concentration is associated with the analog synthesis. The DPN analog has been isolated from tumor tissue and identified.

5) The results are discussed with respect to the significance of enzymatically catalyzed exchange reactions in chemotherapy.

References and Notes

1. The abbreviation DPN is used for diphosphopyridine nucleotide. In the formula NRPRA, N is nicotinamide, R is ribose, P is phosphate, A is adenine, X is a pyridine compound related to nicotinamide.
2. L. J. Zatman *et al.*, *J. Biol. Chem.* **209**, 453 (1954).
3. —, *ibid.* **209**, 467 (1954).
4. —, *J. Am. Chem. Soc.* **75**, 3293 (1953).
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6. —, in preparation.
7. Contribution No. 93 of the McCollum-Pratt Institute. This work was supported in part by grants from the American Cancer Society as recommended by the Committee on Growth of the National Research Council, the Williams Waterman Fund, the American Trudeau Society Medical Section of the National Tuberculosis Association, and the Rockefeller Foundation.
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9. A. Goldin, S. R. Humphreys, and J. M. Venditti, in preparation.
10. It is of interest to note that Ackermann and Taylor (11), in their studies of the toxicity of acetyl pyridine on embryonic chicks, found that nicotinamide reversed the toxicity competitively, whereas nicotinic acid and tryptophan had only a slight effect. Furthermore, in Woolley's experiments (8), a protective action of nicotinic acid on acetyl pyridine toxicity in mice occurred only when the acid was prefed. Simultaneous administration of the acid with the acetyl pyridine was not effective.
11. W. W. Ackermann and A. Taylor, *Proc. Soc. Exptl. Biol. Med.* **67**, 449 (1948).
12. L. J. Zatman, N. O. Kaplan, and S. P. Colowick, *J. Biol. Chem.* **200**, 197 (1953).
13. LD₅₀'s and standard error calculated by Kärber's method as described by Cornfield and Mantel (14).
14. J. Cornfield and N. Mantel, *J. Am. Stat. Assoc.* **45**, 181 (1950).
15. N. Mantel, personal communication.
16. E. G. McDaniel, *Federation Proc.* **12**, 472 (1953).
17. O. H. Gaebler and W. T. Beher, *J. Biol. Chem.* **188**, 343 (1951).
18. W. T. Beher, W. M. Holliday, and O. H. Gaebler, *ibid.* **188**, 573 (1953).
19. W. T. Beher and W. L. Anthony, *ibid.* **203**, 895 (1953).
20. A detailed description of the conditions and kinetics that are involved in the conversion of nicotinamide to DPN will be given elsewhere.
21. The acetyl pyridine analog was determined by its resistance to Neurospora DPNase. The method used for this determination, as well as that for DPN, will be described in detail in a subsequent publication.
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Walter S. Hunter: Pioneer Objectivist in Psychology

IN the death of Walter S. Hunter, psychology lost one of its most distinguished and useful men. Although his contributions were many and varied, they had one thing in common: an effort to develop psychology as a natural science. This attitude toward his chosen field dates back to his own undergraduate days when he saw to it that he was adequately prepared in the basic sciences. It persisted throughout his life, for his most recent graduate students were still required to make up any deficiencies in mathematics, chemistry, physics, and biology before they got very far toward the doctorate in psychology.

Hunter early realized that if psychology were to be a natural science, it had to use objective methods. Hence, he was one of the first scholars to turn away from the study of subjective mental processes to the observation of animal behavior; his doctoral dissertation at the University of Chicago was a study of the delayed reaction, a technique that furnished objective evidence of symbolic processes in the lower animals. His later work with double alternation was aimed in the same direction. But he did not confine his research to animals, for he saw that human, as well as animal, learning could be studied objectively. Indeed, there are few topics in psychology in which he has not done some research—and all of it is characterized by the ability to see an important problem and to tackle it by an efficient and objective method. The net result was a steady stream of substantial contributions, with none of the extreme views that were so likely to appear in the writings of the other early behaviorists; for example, Hunter never fell in with the extreme position of attributing all development of behavior to learning and denying the existence of instincts.

This wariness of extreme positions may be attributed to his "common sense," one of his outstanding attributes; it is probably one of the reasons he never established a "school" or system of psychology. But the sensible and direct way in which he always tackled problems made him a very effective representative of psychology as a science.

One of his most important services to psychology was a pioneer effort in documentation. In 1927 he established the *Psychological Abstracts* and carried on this service until 1947. It was a great success from the start, perhaps because he made an extensive trip abroad to set up an international board of editors before he started work on the first number. It is difficult to imagine how we would get along without this publication, for from the start it has abstracted every paper related to psychology, regardless of the language in which it was written. He stayed on as editor until the *Abstracts* was thoroughly established and then let it pass on to younger hands.

In the 1930's he became a national figure, serving as president of the American Psychological Association and as a member of the National Academy of Sciences and was active in the National Research Council.* After his experience with the Army testing program in World War I, it was natural for him to take the lead in turning psychology to use as World War II approached. At first these efforts were largely on a committee and consultative basis, but in 1943 he was unofficially "drafted" to direct and coordinate much of the extramural research for the services. As chief, Applied Psychology Panel, National Defense Research Committee, he performed invaluable service in keeping psychologists working as teams and in explaining their efforts, abilities, and results to other scientists and to the armed forces. Perhaps nobody will ever know all he did during these years, but it was obvious that he earned the President's Medal of Merit, which was presented in 1948.

After the war, his services were still in great demand on the national scene. He had the rare ability to sit back at a conference, quietly take in opposing views, and then present a clear and logical synthesis of the problem at hand. This very useful trait seems to have functioned as effectively in high-level conferences as it did in local meetings at Brown University. But after he turned 60, Dr. Hunter gradually gave up the activities that demanded extensive traveling, largely on the theory that they should be in the hands of younger men, anyway. He did continue to be active in AAAS and the American Philosophical Society to the end of his life. As he dropped outside responsibilities, he had more time to enjoy his university functions, his home, and his painting—he was an enthusiastic and able amateur painter. It was particularly fortunate that his students and associates presented him with funds to have his portrait painted last spring, for he had a very interesting time sitting for it, and he was able to see and approve the finished project before his death.

No account of Dr. Hunter would be complete without telling of his relations with his students and junior associates. His laboratories at Clark (1925-36) and at Brown (1936-54) were always active in research and graduate instruction, but the number of people involved was kept small, so the group was always an intimate one. He avoided conflict and tension by making each person compete with "par" rather than with his associates. That is, Dr. Hunter sized up the abilities of each person and assigned him tasks of appropriate difficulty. Furthermore, once the task was as-

* For further details, see his autobiography in *A History of Psychology in Autobiography*, Langfeld et al., Eds. (Clark Univ. Press, Worcester, Mass., 1952), vol. IV, pp. 163-187.

signed, Dr. Hunter let the person carry it out on his own. It must have been hard at times to watch people bungle, but it certainly promoted their growth and independence to be forced to find their own way through the problems of research, teaching or administration. As a result, Hunter's students and associates have a deep admiration and fondness for him, yet all have developed along the lines of their own interests rather than following a path he laid down.

Fortunately, Dr. Hunter was in excellent health until the end. On 22 March, his 65th birthday, he resigned the chairmanship of the Brown department of psychology but he looked forward to another 5 years of teaching and research. In July he took an extensive

motor trip with Mrs. Hunter. A few days after his return to Providence he had what appeared to be a slight coronary occlusion and went to the hospital as a precautionary measure. Two days later, on 3 August, he had another attack, and died that evening.

We all feel keenly the loss of this wise leader and kind friend. There is consolation in the knowledge that his life was full and satisfying. And we must remember that he always taught us to devote our full energies to the job ahead; the greatest tribute we can pay him is to continue building on the solid foundations he laid.

HAROLD SCHLOSBERG

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News and Notes

Soviet Astronomy

This report attempts to convey our impressions of some of the scientific institutions in Leningrad and Moscow gathered during a recent, but unfortunately very brief, visit [*Science* 119, 794 (4 June 1954)]. We traveled to Russia in order to participate in an international astronomical meeting in connection with the dedication of the rebuilt Pulkovo Observatory, which is located on the outskirts of the city of Leningrad. The invitation to attend this meeting came from the president of the Academy of Sciences of the Soviet Union. From western Europe, 10 astronomers attended, from Canada and Mexico, one each, while the representation from countries behind the iron curtain, not including Soviet Russia, numbered about 40, not all of whom were astronomers. During our 16-day stay in Russia, we were given the opportunity to visit various scientific institutions.

Dedication ceremonies of the observatory were held from 20 to 22 May and included addresses dealing with its history and current work in several fields of research. These were followed by 3 days of symposiums, one on "Astrometry" and the other on "Variable stars," during which we were invited to present papers.

Pulkovo Observatory has a distinguished history, particularly in the field of astrometry. It was established in 1839 and in 1885 possessed the largest telescope in the world, a 30-in. refractor. During World War II its buildings were completely destroyed. However, most of the instruments and the greater part of the library were saved. The Kepler manuscripts and other historical papers, which were in the library, are now in the Academy Building in Leningrad. The mounting of the large refractor was destroyed, but the lens was saved. In its place a 26-in. refractor is to be mounted in a building that is now approaching completion. This instrument was constructed in Germany.

The present telescopic equipment of the observatory consists principally of the carefully reconditioned old

instruments and a few new, but small, instruments made in Leningrad. These latter are a fixed-tube polar telescope to study the motion of the celestial pole among the stars, a beam-type interferometer for measuring the angular separation of double stars, a Maksutov-Schmidt telescope to be used for photoelectric spectrophotometry, and a number of still smaller instruments. The objectives of these telescopes have diameters of less than 24 in. The horizontal solar telescope is well equipped with interference filters, gratings, and photoelectric registrations.

The auxiliary equipment of the observatory—such as crystal clocks, stellar photometers, microphotometers, and comparators—is new and was constructed in Leningrad. We understand that a 19-stage multiplier is used in connection with the photoelectric equipment. The observatory is staffed with 75 scientific workers and has a total personnel of 200. Housing is now being made available for the staff on the grounds of the observatory.

The Institute for Theoretical Astronomy at Leningrad performs functions that correspond to those of the Nautical Almanac Office in Washington and similar offices in other countries. This institute concentrates much of its effort on the computation of ephemerides of minor planets and publishes an annual volume of these ephemerides. This work is facilitated by the use of an elaborate set of punched-card machines, which includes four or five tabulators and five multipliers. The latter are not of the most modern type now in use in the United States, and we did not see an electronic computing machine.

The University of Moscow, which without doubt is the leading institution of higher education in the Soviet Union, is undergoing a phenomenal growth. The present building activities are concentrated outside the city limits. More than 30 buildings have been completed and a number of others are under construction. Some of these buildings are large skyscrapers. The old university buildings near the Kremlin continue to house the humanities, law, and medicine. The new buildings house the departments of science,

together with living quarters for the instructional staff and for 6000 students. Each student occupies a separate room in a two-room suite. A number of theaters, swimming pools, and other recreational facilities are provided. The principal building houses the central library as well as the department libraries. Separate reading rooms for graduate and undergraduate students are provided.

The total enrollment of the university is 18,000 students, of which 4000 are students by correspondence. The number of science students is 8000, of which 1500 are in the graduate schools. This does not include students in engineering. Special institutions provide instruction in technology. Admission to the universities is by high-school diploma, although Moscow accepts only one out of five applicants. Young people from all over the Soviet Union seek admission, 67 nationalities being represented in the university. Women students are more numerous than men. Admission to the graduate school requires, in addition to scholastic attainments, the passing of an examination on the political philosophies of Marx and Lenin.

The undergraduate studies extend to 5 yr and an additional 3 yr are required for a student to receive training equivalent to the doctorate. The greatest proportion of students receive from the state adequate stipends for living expenses. A graduate student receives about twice what an undergraduate receives, plus additional funds for books. Last year's enrollment in the division of mechanics and mathematics, which includes astronomy, was 400 graduate students. This year 19 have received diplomas in astronomy. A staff of 12, of which 5 are professors, is provided in this field. Instruction is given in astrometry, geodesy, and astrophysics.

Observational astronomy in Moscow is centered around the Sternberg Institute, established in 1831, and at present occupying overcrowded quarters in the city. Its staff is composed of 110 workers of which 60 are scientists. The largest instrument at this observatory is a 13-in. astrograph and is used primarily for the determination of proper motions of stars. As in the case of Pulkovo Observatory, astrometry is emphasized and a number of meridian instruments and clocks are in operation. The time service of the Soviet Union is entrusted to this institution. A new 100-mm broken transit, the first to be built in Russia, is to be used for the determination of time. It is to be equipped to register star transits photoelectrically. Another new telescope now in operation is a small, 18 by 20 in. Maksutov-Schmidt-type instrument that is provided with objective prisms. The library of the observatory contains 40,000 volumes. One of the principal services of the institute is the preparation and publication of the *General Variable Star Catalogue*, an indispensable publication for many workers all over the world.

This fall the observatory is to be moved into its new and spacious quarters near the new university buildings, and it will be equipped with all new, but small, instruments including a small solar telescope. The primary function of the Sternberg Institute is

to serve as a training center for the university students specializing in all branches of astronomy. As a matter of fact the principal members of its staff are professors at the university. Plans for a research center in astronomy are now going forward at a location 40 km from the city. It is hoped that it will be completed by 1960.

It is difficult to evaluate the over-all activities in astronomy in the Soviet Union. This is partly due to the language barrier. The fact that the Soviets have trained and are training a large number of astronomers is evident. Their output in publications is enormous, both in journals and in popular and advanced books in astronomy. Nearly every observatory or institute has its own publication series. From the standpoint of equipment they are deficient, but the indications are that they are determined to build their own instruments. The largest telescope in operation at present is a 50-in. reflector. The largest refractor has a diameter of 26 in. Both instruments are of German make. Likewise no significant large Schmidt-type telescopes are in operation or are planned for the near future. We have no knowledge of the existence of any radio telescopes.

During our brief visit to Russia, the Soviet astronomers were most helpful and always ready to make us acquainted with their work and their instruments. The Soviet Academy, our host, made our stay very pleasant and comfortable. The translators assigned to us proved very efficient and eager to help us. We are grateful to all of them. We are also indebted to the National Academy of Sciences for making the necessary arrangements in securing our passports and visas and to the National Science Foundation for travel grants so generously provided.

J. J. NASSAU

DIRK BROUWER

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Science News

An editorial in the 9 Aug. issue of *Chemical and Engineering News* protests salary discrimination against Ph.D. scientists in the armed forces and the Public Health Service. Physicians, dentists, and veterinarians holding active commissions in these fields of government service receive by law \$100 a month more than is paid to chemists and other scientists with the Ph.D. degree who hold similar commissions.

... we feel that all the arguments advanced to support extra pay for physicians and dentists and, particularly veterinarians apply equally well to chemists and other scientists. . . . In government facilities such as the Public Health Service's National Institutes of Health, physicians and dentists are often engaged in research projects exactly the same as those carried out by chemists, biochemists, and other scientists. In some such cases project directors are scientists and some of the subordinates are physicians and dentists. Yet the latter get \$1200 a year more than their project supervisors.

We believe that in all fairness Congress should give equal treatment to government employees with comparable education, training, and experience. This could be done by extending the provisions of Public Law 84 to cover scientists who hold earned doctor's degrees and who hold active commission in the Armed Services or the Public Health Service.

A new high-flux reactor for fundamental research and engineering studies is to be constructed at the Atomic Energy Commission's Oak Ridge National Laboratory for an estimated \$2,800,000. The reactor will have a heterogeneous core with enriched uranium as fuel. It will use ordinary water as a moderator and coolant, and will operate at a power level of 5000 kw.

In delivering the presidential address of the British Association for the Advancement of Science, E. D. Adrian, president of the Royal Society and master of Trinity College, Cambridge, warned that

We must face the possibility that repeated atomic explosions will lead to a degree of general radioactivity which no one can tolerate or escape. Unless we are ready to give up some of our old loyalties we may be forced into a fight which might end the human race. Our predicament is the inevitable result of our curiosity and of the physical nature of the world we live in, but if we can make our behavior worthy of our increased knowledge we can live safely.

The scientist, therefore, has a double responsibility. He must apply his science to learn as much as possible about the mental and physical causes which make us behave as we do, he must study human nature to prevent its failures. But he cannot wait for the discoveries which might make us act more wisely: he must take us as we are and make it his task to point out that the human race cannot stand more than a few thousand large atomic explosions whether they hit their target or miss it.

If we must continue to make war there is no kind of scientific investigation which might not be used to make it more effective. There can be no guarantee that discoveries in the field of human conduct would be harmless. A drug or a system of education which would make us all do as we are told, a method of producing radical conversion to a new system of belief, a knowledge of new ways of rousing patriotic ardor, all these might be used with consequences almost as grim as the genetical deterioration in a radioactive world. The psychiatrist who discovers a cure for paranoia may find that he has also revealed a convenient way of producing it.

Discoveries relating to our own nature may mean a painful readjustment of our beliefs, Adrian observed. He recalled the great discussion over Darwin's theory of natural selection 100 yr ago and drew a close parallel with the impact of Freud's theories on our own generation.

The theory of unconscious forces moulding our thought has certainly diminished our stature as intelligent beings. Yet the parallel still holds, for again we have recovered our equanimity. We are reconciled to the unconscious, though we may not have digested all the elaborations of psychoanalytic theory. We are no doubt less sure of ourselves, inclined to spare the

rod and to put nothing in its place, but, on the whole, Freud has left us with a better understanding of human conduct and we are not down-hearted at finding it less rational than we used to suppose.

Adrian urged that there be more investigations in the field of the social sciences, even though it is difficult for those who study social activities, so enmeshed with human actions, to do controlled experiments. Even after it is discovered what is likely to happen in a particular situation, the statesman who consults an expert may not be able to act to prevent trouble. Adrian commented that we may find out a great deal about the tensions which lead to war without seeing the way to keep ourselves clear of it. He is optimistic about the future, however.

We are constantly acquiring new habits and new ways of thought. It does not take us very long to see the way round old quarrels. Darwin and Freud no longer trouble us. We are no doubt born with brains like those of our remote ancestors and when we are grown up we have no more native intelligence than they had, but our brains must have been so modified by what we have learned that they are physically and chemically different, better adapted for the complex social life of our time. We have more knowledge at our disposal. If all goes well with our training the brains we have ought to be more civilized than those of our fathers and those of the next generation, more civilized than ours.

The *Journal of the American Medical Association* for 7 Aug. contains an account of the relationship between smoking habits and human death rates by E. C. Hammond and D. Horn of the medical and scientific department, American Cancer Society. These workers present preliminary findings, covering about 20 mo, of a follow-up study of 187,776 men between the ages of 50 and 69. The available information indicates that the over-all death rate, the death rate from diseases of the coronary arteries, and the death rate from cancer, are all much higher among men with a history of regular cigarette smoking than among men who never smoked.

The workers state that the findings prove a definite association between smoking habits and death rates, and feel that the associations found between regular cigarette smoking and death rates from coronary artery disease and lung cancer reflect cause and effect relationships.—E. M. L.

J. C. Bartlet and C. G. Farmilo of the Food and Drug Laboratories, Canadian Department of National Health and Welfare, Ottawa, have discovered that the geographic origin of raw opium can be determined by chemical analysis of the ash when the opium is burned. Knowing the source of the drug should help tighten control measures and suppress illegal production. The investigation, which was a UNESCO project, was reported in the 27 Aug. issue of *Nature*.

The Canadian research group has analyzed more than 100 opiums—from Yugoslavia, two regions in Turkey, Iran, India, Indo-China, Korea, and China. Tests were made for both major and minor constituents. The elements determined were potassium, cal-

cium, phosphorus, sodium, magnesium, silicon, iron, aluminum, titanium, boron, manganese, molybdenum, lead, tin and copper. Spectrographic, colorimetric and flame photometric procedures were used.

The latest nationwide tabulation of statistics on **mental patients in public hospitals** shows that 622,000 persons were on the books at the end of 1952. A year earlier the figure was 610,000. The end-of-year figures for 1952 listed just under 100,000 patients for New York State's public hospitals for the mentally ill—more than double that of the next highest state total. The comprehensive tabulation is titled *Patients in Public Hospitals for the Prolonged Care of the Mentally Ill, 1952*, and is the third of a series of such reports prepared by the National Institute of Mental Health's Biometric Branch. It is available from NIMH; specify "Current Reports Series IMH-B54—No. 1."

Ground granite can be used as a fertilizer according to results of a research program being conducted by Charles J. Lyon, chairman of the Dartmouth College botany department, with the aid of the New Hampshire State Planning and Development Commission. Lyon's studies show that the minerals feldspar and mica, both common ingredients of granite, may be useful as potassium fertilizers for a variety of plants. This is particularly significant not only for New Hampshire, the "Granite State," but for many other parts of the nation where crop soils are deficient in potassium, which is one of the three main fertilizer elements.

However, a number of crop plants tested—such as tomatoes, sweet corn, and tobacco—cannot utilize this potash mineral. Why these do not benefit and legumes do is a question that is still to be answered.

The problems caused by the contact of modern civilization with culturally more primitive societies are acute ones that have led to assimilation, depopulation or extermination of many of the native groups. Nowhere is this more evident than among the Pacific islands. A study of the factors involved in the **depopulation of Yap**, an island group of western Micronesia with an area totaling 38.67 mi² enclosed within a single coral reef, is therefore especially pertinent. E. E. Hunt, Jr., N. R. Kidder, and D. M. Schneider have reported results of a Harvard expedition of 1947-48 correlated with other available data [*Human Biol.* 26, 21 (1954)].

The population of Yap prior to its annexation by Spain is not known, although on theoretical grounds it may have been as much as 51,000; the authors, however, regard this estimate as probably excessive. Over a century ago, the Yapese began to decrease in numbers. The first census, in 1899, showed a total of 7808. Under subsequent German and Japanese occupations the population steadily decreased, so that in 1946, one year after U.S. occupation, it numbered only 2582. Subsequently, it has undergone a slight increase.

The authors conclude that increase in mortality,

chiefly as a result of severe infectious diseases, probably started the population decline. Even after several decades of foreign rule the crude death rate was still high; from 1917 to 1930 (under Japan) it was about 40 per 1000. The crude birth rate during the same years was only about 15 per 1000, so that depopulation continued unabated. The low birth rate seems not to be explained by the absence of men from Yap; indeed, permanent immigration and emigration apparently have had no appreciable effect on the depopulation rate. The low birth rate may be partially explained by the high frequency of genital pathology and intestinal parasites. However, numerous Yapese cultural patterns seem to have limited fertility.

Since American occupation the crude birth rate has doubled and the crude death rate has halved. Health has improved, and several social and cultural changes have apparently helped to increase fertility. The authors conclude that with improved health and sanitation and a high morale, the population of Yap will probably continue to increase moderately.—W. L. S., Jr.

According to a brief communication in the *Physical Review* for 15 July, Atterling, Forsing *et al.* of the Nobel Institute of Physics, Stockholm, have used the 225-cm cyclotron to produce a beam of high-energy oxygen-16 ions sixfold charged, of energy approximately 180 Mev, and current about 0.03 μ amp. By bombarding uranium with this beam, they found an activity that is ascribed to the new element 100 with a half-life of 0.5 hr. From alpha particle emission theory, they conclude that their data for alpha disintegrations with an energy of 7.77 Mev correspond to an atomic mass of about 250.—K. L. H.

Scientists in the News

Robert W. Allard, University of California agronomist at Davis, has left for a year's study in Europe. He will be a Fulbright senior research scholar at the University of Birmingham's Biometrical Laboratory, in England, for most of his stay abroad. There he hopes to find answers to certain problems that will help him and other plant breeders develop higher-yielding, disease-resistant crop varieties better adapted to various growing conditions.

Ross H. Arnett, Jr., entomologist for the U.S. Department of Agriculture and curator of insects at the U.S. National Museum, has been named associate professor of biology at St. John Fisher College, Rochester, N.Y.

Marvel L. Baker, associate director of the Nebraska Agricultural Experiment Station (Lincoln), and **Truman E. Henton**, head of the Department of Agriculture's farm electrification section (Beltsville, Md.), have been elected members of the Scientific Manpower Commission. Their election increases the membership of the commission to 18.

New members of the board of trustees of Biological Abstracts, Inc., are **Stanley A. Cain**, chairman of the department of conservation at the University of Michigan; **H. Bentley Glass**, professor of biology at the Johns Hopkins University; and **William B. Sarles**, acting chairman of the department of bacteriology at the University of Wisconsin.

Two surgeons originally trained at the University of Chicago are returning to serve in the university's department of surgery. **Joseph P. Evans**, associate professor of surgery in charge of neurosurgery at the University of Cincinnati Medical School, will become professor of neurosurgery, and **John Van Prohaska**, formerly professor of surgery at the University of Illinois, has been appointed professor of surgery.

John M. Fogg, Jr., professor of botany and since 1 July director of the Morris Arboretum of the University of Pennsylvania, has recently returned from a 2-mo visit to India where he went to collect plants for the Arboretum.

Victor H. Fraenckel, former liaison scientist in physics at the General Electric Research Laboratory, Schenectady, N.Y., has been appointed consultant on scientific relations. He will be responsible for informing and counseling the management of the laboratory regarding scientific work under way outside the General Electric Co.

Jack Gross, associate professor of anatomy at the New York State University College of Medicine in Brooklyn, received the 1954 Chilean Iodine Educational Bureau award in Boston, Mass., at the 101st convention of the American Pharmaceutical Association. The ward of \$1000 and a citation certificate was given to Gross for his fundamental contributions in the field of iodine that have revised the entire concept of the metabolism of the thyroid hormone. Gross has demonstrated the presence of a new iodine compound, triiodothyronine, in human blood. Together with R. Pitt-Rivers at the National Institute for Medical Research, London, he isolated triiodothyronine from the thyroid of cattle, explored its physiological properties and synthesized it chemically, making it possible to test its effects on the body.

Robey W. Harned, one of the founders of professional entomology in the South and long a leader in cotton insect research, retired from the U.S. Department of Agriculture at the end of July after having directed cotton insect work for the Bureau of Entomology and Plant Quarantine for more than 20 yr. Since the department's reorganization last fall he has been acting as consultant and staff assistant to the chief of the Entomology Research Branch, Agricultural Research Service.

Prior to his federal employment, Prof. Harned was for 25 yr professor of entomology and zoology at Mississippi A. & M. College and entomologist at the

Mississippi Agricultural Experiment Station. He also was in charge of state nursery inspection and of regulatory and extension work, served as executive officer of the Mississippi State Plant Board from the time of its organization in 1918, and did research on cotton, scale, and pecan insects. Prof. Harned was honored 16 July by friends and associates—many of them ex-students—and among the gifts presented to him were a vacation check for \$800.00 and a collection of some 300 letters from friends in 26 states and 3 foreign countries. The Cotton States Branch of the Entomological Society of America, of which he is a past chairman, honored him at a banquet in Biloxi, Miss., last January.

Takeru Higuchi, associate professor in the University of Wisconsin School of Pharmacy, is 1954 winner of the Ebert medal for outstanding pharmaceutical research. He received the honor for significant investigations in the physicochemical aspects of pharmacy, with specific reference to his work on the physics of tablet compression and on the complexes formed in solution by caffeine. Two former Wisconsin graduate students share in the honors as Higuchi's coworkers: **A. Narsimha Rao**, now in charge of laboratories in the Indian Division of Parke, Davis and Co.; and **D. A. Zuck** of Eli Lilly and Co. Both received certificates of honorable mention.

Following 4 yr of service with Bell Telephone Laboratories, **Thomas R. Hoffman** has become an associate professor of electrical engineering at Union College, where he had previously been a faculty member.

Aviation's Daniel Guggenheim medal will go this year to **Clarence Decatur Howe**, Canadian engineer and Minister of Trade and Commerce and Minister of Defense Production. Presentation will be made in Los Angeles, 8 Oct., at a session of the National Aeronautic meeting of the Society of Automotive Engineers, which sponsors the award jointly with the American Society of Mechanical Engineers and the Institute of the Aeronautical Sciences.

Howe, a native of Waltham, Mass., and a 1907 graduate of M.I.T., is being honored for "initiating and organizing commercial air routes and services, promoting aeronautical research, development and production of aircraft and engines, and advancing the art of aeronautics." He is a civil engineer who as a Canadian cabinet minister since 1935 has been responsible for most of his government's developments in aviation.

William T. Ingram has established a consulting practice in sanitary engineering in New York. He will continue his association with the New York University College of Engineering as adjunct professor.

Waldemar Kaempffert of the New York Times is this year's Kalinga prize winner. The prize is awarded annually through UNESCO from the endowment of P. Patnaik, a member of the legislative assembly of

the state of Orissa, India. The Kalinga Trust Fund was set up in 1951 to emphasize the importance of the competent presentation of science to the public and to establish a cultural contact between India and the scientifically advanced nations. The winner will attend the annual meeting of the Indian Science Congress and spend a month in India lecturing at scientific and public meetings. The official UNESCO announcement stated that Mr. Kaempfert was nominated by the British Association of Science Writers and was chosen from among 10 nominees from Austria, Brazil, France, Germany, Great Britain, India, Peru, Venezuela and the United States.

B. Marr Lanman has been appointed head of clinical research for Schenley Laboratories, Inc. Before joining Schenley in 1952, Lanman was resident in thoracic surgery at Presbyterian Hospital in New York.

William C. Moloney, on leave of absence for 2 yr while serving as director of the medical research program for the Atomic Bomb Casualty Commission in Hiroshima, Japan, has returned to the Boston City Hospital where he has been appointed director of the Clinical Laboratories. Moloney will also continue his position as clinical professor of medicine and assistant director of the first and third medical services (Tufts) at the Boston City Hospital.

The University of Michigan has announced the dismissal of **Mark Nickerson**, associate professor of pharmacology in the Medical School, and **H. Chandler Davis**, instructor in mathematics in the College of Literature, Science, and the Arts. Simultaneously the reinstatement of **Clement L. Markert**, assistant professor of zoology, was announced. All three were suspended on 10 May when they refused to answer questions by the U.S. House Committee on Un-American Activities about alleged membership in the Communist party. The committee was headed by Rep. Kit Clardy of Michigan. Davis relied only on the First Amendment and has since been cited for contempt of Congress. He was indicted by a Federal District Grand Jury in Grand Rapids on 25 Aug. on 26 counts. These actions were not under consideration by any university group investigating Dr. Davis's case. Nickerson and Markert refused to answer the committee on the grounds of the Fifth Amendment.

An advisory committee of the university senate, made up of five faculty members, unanimously recommended the dismissal of Davis, as did a special appeal committee known as the Committee on Intellectual Freedom and Integrity. Davis would answer no questions about his alleged membership in the Communist party.

The university advisory committee voted three to two for Nickerson's reinstatement with severe reprimand and the Committee on Intellectual Freedom and Integrity supported that recommendation unanimously; however, the dean and executive committee of the Medical School, where Dr. Nickerson taught and carried on research, unanimously recommended his

dismissal. Before both faculty committees, Nickerson admitted former membership in the Communist party, but he said he had gradually withdrawn between 1944-45 and 1947-48, primarily because he did not have time to carry on the party's work. This weighed heavily in the decision to recommend dismissal.

All committees investigating the Markert case were convinced that his one-time membership in the Communist party, when he was young, and his subsequent membership in the party and his withdrawal from it, and his present attitude toward the party are all of such a nature that there is no justification for his summary dismissal as the facts are now before the university. A letter of censure was authorized.

Harold H. Plough, head of the department of biology at Amherst College, has been appointed to serve for the balance of the late Joseph H. Bodine's term as secretary of AAAS Section F—Zoological Sciences. The term runs through Dec. 1955.

Meetings

Announcement is made of the **First Electronic Computer Clinic**, to be held in conjunction with the First International Automation Exposition at the 244th Regiment Armory in New York, 30 Nov.-2 Dec. (The exposition opens 29 Nov.) The clinic is a lecture and demonstration course planned for top management, management and production engineers, physicists, chemists, and others who contemplate using digital or analog computers in the plant or laboratory. Advance registration (fee, \$5) is required. Forms can be obtained from Richard Rimbach, Electronic Computer Clinic, 845 Ridge Ave., Pittsburgh 12, Pa. Registration will not be accepted from individuals employed by computer manufacturers.

The first five lectures of the **Harvey Society's 50th anniversary series**, to be given under the patronage of the New York Academy of Medicine at its headquarters, are as follows:

23 Sept., "Hormones of the posterior pituitary gland: oxytocin and vasopressin." Vincent du Vigneaud, professor of biochemistry, Cornell University Medical College.

14 Oct., "The metabolism of the heart." Richard J. Bing, professor of experimental medicine and clinical physiology, Medical College of Alabama.

18 Nov., "Lipoproteins of human plasma." J. L. Oncley, professor of physical chemistry, Harvard University.

16 Dec., "Control and interrelations of metabolic and viral diseases of bacteria." André Lwoff, head of the department of microbial physiology, Pasteur Institute, Paris.

20 Jan., "The intermediary metabolism and biological activities of ferritin." Ephraim Shorr, associate professor of medicine, Cornell University Medical College; and research associate, Russell Sage Institute of Pathology.

The fall meeting of the **Operations Research Society of America** is to be held at the Sheraton-Park Hotel in Washington, D.C., 19-20 Nov. The program will consist of symposiums on the accomplishments of operations research in industry, dynamic programming, and the use and value of war-game methods in solving operations research problems. In addition to sessions of contributed papers, papers on theoretical developments have been invited.

The 5th annual scientific meeting of the **Society for Clinical and Experimental Hypnosis** will take place on 30 Oct. at the New York Academy of Sciences. Inquiries about membership in this society should be addressed to the president, Jerome M. Schneek, 26 W 9 St., New York 11.

This country's first society for scientists and engineers working in the atomic energy field has been formed. It is known as the **Society of Nuclear Scientists and Engineers**. The purpose of the organization is to foster the "integration and advancement of nuclear science and technology primarily through the holding of meetings and the publication of papers." SNSE's first major activity will be a 3-day technical conference to be held in June 1955 at Pennsylvania State University.

The society has been organized by a group of 27 scientists and engineers from every important atomic energy installation in the country.

The organizing committee for SNSE was established on 10 Dec. 1953, and the first 6 mo of 1954 were spent in intensive investigation to determine the need for an independent society. Details about membership can be obtained from Dr. Urner Liddel, 1104 Fisher Bldg., Detroit, Mich.

The **Society of Rheology** will hold its annual meeting in Washington, D.C., 3-5 Nov. The technical sessions will take place at the National Bureau of Standards, and the headquarters hotel will be the Sheraton Park. Four main groups of papers are scheduled: (i) time dependent mechanical behavior of monomeric liquids, elastomers, plastics, glass, and asphalts; (ii) statistical and molecular theories of liquids with particular regard to rheologic processes; (iii) volumetric strain in monomeric liquids, glass, and organic polymers; and (iv) critical velocities and impact strength, anisotropy, and chemically induced relaxation of fibers. In addition, individual papers will be given on a wide variety of rheologic topics.

Among the 25 authors scheduled to deliver papers are: Henry Eyring of the University of Utah; R. B. Lindsay, A. H. Lee, and R. S. Rivlin of Brown University; Charles Mack of Imperial Oil Limited, Sarnia, Ont., Canada; A. Michels of the University of Amsterdam, Holland, and the University of Maryland; Melville Green of the University of Maryland; Simon Rodbard of Michael Reese Hospital, Chicago; and C. van der Poel of Royal Dutch Shell, Amsterdam, Holland.

An informal dinner on 4 Nov. will feature the

award of the society's Bingham medal, and an address by Alan T. Waterman, director of the National Science Foundation, on the general subject of government support of research. Further information about the meeting can be obtained from F. D. Dexter, Bakelite Company, Bound Brook, N.J.

Dedication ceremonies for the new \$10 million building of the **University of Texas M. D. Anderson Hospital and Tumor Institute** in the Texas Medical Center, Houston, will be held 23 Oct. The ceremonies will be preceded by a 3-day program for general practitioners and laymen.

Education

The first course in **air pollution** to be given in New Jersey will be inaugurated this fall by **Rutgers University**. It will be a general and beginning course and will be open to qualified persons from industry and governmental agencies as well as to undergraduate and graduate students.

A research team at Oberlin College (Ohio) has begun a study of **preparation for medical education in a liberal arts college**, aided by a grant from the Commonwealth Fund of New York. While medical schools are encouraging prospective students to gain a liberal educational background, little is known about the progress in medical schools of students with such backgrounds as compared with students whose undergraduate programs have been heavily weighted with premedical courses.

The University of Oklahoma's School of Journalism has prepared a 4-yr curriculum for premedical students or newspaper men interested in **science journalism**. It is designed to aid in the preparation of scientific papers and to help the premedical student who ultimately pursues another career.

Successful operation of a program in correlating the **teaching of pathology** with other disciplines in the University of Kansas Medical School has been reported in the September *Journal of Medical Education* by Robert E. Stowell, chairman of the departments of pathology and oncology.

This fall the **University of California Extension** will inaugurate a course in "Application of the principles of industrial medicine to private practice." Requests for information should be made to Thomas H. Sternberg, Division of Postgraduate Medical Education, University of California Medical Center, Los Angeles 25.

A **wind tunnel** especially designed for heat transfer studies just below the speed of sound will be constructed at **Illinois Institute of Technology** under an Air Force research contract. Purpose of the studies will be to gather basic information which can be used

in such problems as de-icing and anti-icing at high subsonic speed levels. The tunnel will maintain a jet of 575 hp. Unlike the better known wind tunnels, this one will be small and relatively inexpensive but will incorporate many of the features of the larger tunnels.

A report on the first 30 yr of the "Yale Plan of Medical Education," a method of study which differs in many respects from that of most American medical schools, appears in the September issue of the *Journal of Medical Education*. Vernon W. Lippard, dean of the Yale University School of Medicine and president-elect of the Association of American Medical Colleges, is the author of the report. The Yale program is based on four characteristics: a required dissertation, lack of fixed course requirements for qualified students, emphasis on elective courses, and the absence of required course examinations. Each student prepares an original hypothesis for the faculty member under whom he chooses to work. From that point on, he is treated as though he were a graduate student, and if he can demonstrate competent knowledge in a particular course, he is excused from attendance and given more time for elective work.

Since instruction is carried out in small groups, facilitating the evaluation of achievement, the necessity for required examinations is eliminated. Lippard feels that the Yale plan has been a success, since the students have established and maintained an excellent record in the national board examinations, successful completion of which is the threshold requirement at Yale for advancing from the preclinical to the clinical years, and for graduation. Yale's record compares favorably with the records of other medical schools.

Available Fellowships and Awards

The division of medical sciences of the National Academy of Sciences-National Research Council is accepting applications for postdoctoral research fellowships for 1955-56. These awards are designed to offer research experience to promising individuals who look forward to investigative careers, and not to provide practical experience in the clinical field. Ordinarily fellowships are not granted to persons over 35 yr of age. The following programs are announced:

Fellowships in cancer research are awarded by the American Cancer Society on recommendation of the Committee on Growth of the division of medical sciences. Awards are available for study in all branches of the biological, chemical, and physical sciences and also for clinical investigation applicable to the study of growth, typical or malignant. Citizens of the United States are eligible.

British-American exchange fellowships in cancer research also are awarded by the American Cancer Society upon recommendation by the Committee on Growth. They are offered to citizens of the United States for advanced study in Great Britain in specialized fields pertaining to the problem of growth. Simi-

lar fellowships are awarded by the British Empire Cancer Campaign to young British scientists for research in the United States.

Fellowships in the medical sciences supported by the Rockefeller Foundation and the Lilly Research Laboratories are administered by the medical fellowship board of the division. Fellows are expected to devote themselves to research in the basic medical sciences. The fellowships administered for the Rockefeller Foundation are open to citizens of the United States and Canada; the Lilly Fellowships only to citizens of the United States.

Fellowships in tuberculosis are also administered by the medical fellowship board under a grant from the National Tuberculosis Association. These awards are designed to promote the development of investigators in fields related to tuberculosis. They are open to citizens of the United States who are graduates of American schools.

Fellowships in radiological research are administered for the James Picker Foundation by the division's Committee on Radiology. The Foundation has expressed particular interest in the support of candidates who propose to carry on research oriented toward the diagnostic aspects of radiology. Appointments are not limited to citizens of the United States.

Applications for any of these programs must be postmarked on or before 10 Dec. Fellowships are awarded in the early spring. Complete details and application blanks may be obtained from the Fellowship Office, National Academy of Sciences-National Research Council, 2101 Constitution Ave., NW, Washington 25, D.C.

Grants and Fellowships Awarded

The following AAAS research grants have been awarded:

Alabama Academy of Science to R. E. Wingard, Alabama Polytechnic Institute. Specific heat and heat capacity of furfural, and so forth.

Ohio Academy of Science to P. Chacharonis, Ohio State University. Protozoa on sphagnum plants in a bog in central Ohio.

Ohio Academy of Science to E. Smith, Akron, Ohio. Life histories of non-cave-dwelling bats.

Ohio Academy of Science to T. D. Howe, Defiance College. Flora of northwestern Ohio.

A series of studies of the distribution of heat generated during the cutting of metals will be carried out during the coming year by Columbia University's School of Engineering under a \$10,000 grant from the American Society of Tool Engineers. This is the first research contract entered into by the society. In discussing the work, Victor Paschkis, adjunct associate professor of mechanical engineering at Columbia and technical director of the university's Heat and Mass Flow Analyzer Laboratory, said "Thermal studies of this nature, which are closely tied in with the question of tool life and efficiency, have been severely limited up to now by the equipment and measurement techniques available."

Georgetown University Medical Center has announced receipt of \$109,885 in research grants. Seven of the 8 individual grants reported were from the U.S. Public Health Service and totaled \$106,537.

The following grants and fellowships have been awarded by the National Tuberculosis Association and its medical section, the American Trudeau Society, for the 1954-55 fiscal year.

Grants

T. L. Badger, Boston City Hospital. Pulmonary physiology.
 V. Bryson, Biological Laboratory, Cold Spring Harbor, N.Y. Genetics of mycobacteria.
 M. I. Bunting, Yale University. Genetics of mycobacteria.
 A. Christie, Vanderbilt University. Histoplasmosis and pulmonary calcification.
 C. Cohen, Jackson Memorial Laboratory. Genetic resistance to tuberculosis in rabbits.
 G. F. Filley, Trudeau-Saranac Institute. Pulmonary function.
 J. E. Forney, University of Southern California. Allergy and serology of tuberculosis.
 B. Gerstl, Veterans Administration, Oakland, Calif. Breakdown of the tubercle bacillus by host tissue as a factor in resistance to tuberculosis.
 E. M. Lincoln, New York University-Bellevue Medical Center. Pathogenesis, prognosis, and treatment of tuberculosis in children.
 M. B. Lurie, University of Pennsylvania. Genetic resistance to tuberculosis.
 C. J. Martin, Firland sanatorium, Seattle. Equality of ventilation in lobes of the lung.
 G. M. Meade and R. S. Mitchell, Trudeau-Saranac Institute. Statistical study of treatment of tuberculosis.
 Q. N. Myrvik, University of Virginia. Tuberculostatic substances in mammalian tissues.
 C. E. Palmer, Division of Chronic Disease and Tuberculosis, Public Health Service, Washington, D.C. Minimal tuberculosis in student nurses.
 E. M. Pappe, Columbia University. Effects of anesthesia during pulmonary resection.
 H. Pope, Duke University. Metabolism of tubercle bacilli.
 S. Raffel, Stanford University. Virulence, immunity, and allergy in tuberculosis.
 L. J. Roth, University of Chicago. Distribution of C^{14} labeled para-aminosalicylic acid in mice and guinea pigs.
 L. D. Scheel, Trudeau-Saranac Institute. Metabolism of isonicotinic acid hydrazide by tubercle bacilli.
 F. B. Seibert, University of Pennsylvania. Antigens of the tubercle bacillus.
 W. Steenken, Jr., Trudeau-Saranac Institute. Maintenance of mycobacterial culture depot.
 K. L. Terplan, University of Buffalo. Pathogenetic studies on human tuberculosis.
 T. R. Watson, Jr., Dartmouth Medical School. Lung function during thoracic surgery.
 H. S. Willis, Gravelly Sanatorium, Chapel Hill, N.C. Vaccination against tuberculosis.
 National Society for Medical Research. Annual contribution to educational program on scientific animal experimentation.
 M. Berthrong, Glockner-Penrose Hospital, Colorado Springs, Colo. Tissue culture studies on resistance to tuberculosis.
 E. Bogen, Olive View Sanatorium, Olive View, Calif. Classification of mycobacteria.
 S. P. Colowick and N. O. Kaplan, Johns Hopkins University. Mechanism of action of isonicotinic acid hydrazide and related compounds.
 M. S. Dunn, University of California, Los Angeles. Chemistry of tubercle bacilli.
 A. Goldman, City of Hope Medical Center, Duarte, Calif. Electrolyte, protein and adrenal function studies in tuberculous patients.
 W. F. Kirchheimer, Northwestern University. Correlation of mycobacterial enzyme and growth inhibition.
 W. McDermott, Cornell University. Host-parasite relationships in tuberculosis.
 R. W. Manthel, Jefferson Medical College. Metabolic studies on C^{14} labeled isoniazid.
 G. Middlebrook, National Jewish Hospital, Denver. Chemotherapy and pathogenesis of experimental tuberculosis.
 P. M. Seeborn, State University of Iowa. Pathogenesis of pulmonary emphysema.

J. E. Sifontes, Sanatorio Alejandro, Puerto Rico. Chemotherapy of primary tuberculosis and tuberculous meningitis in children.

D. N. Walcher, Indiana University. Enzyme therapy in tuberculous meningitis.

J. J. Waring, Fitzsimmons Army Hospital and Colorado General Hospital, Denver. Minimal tuberculosis in military personnel.

L. E. Wood, University of Kansas. Tuberculin-histoplasmin rates as an indication of the prevalence of infection in Kansas City, Mo.

Fellowships

C. M. Coleman, National Jewish Hospital, with G. Middlebrook. Chemotherapy of tuberculosis, with special reference to mode of action of isonicotinic acid hydrazide.

A. J. Crowe, Stanford University, with S. Raffel. Immunizing factors of the tubercle bacillus.

National Research Council. Reimbursement for increased increments and administrative costs on current and past fellowships.

National Research Council. Research project at choice of applicant, candidate to be chosen by NRC.

In the Laboratories

A research program in molybdenum chemicals has been launched by the Climax Molybdenum Co. with a \$250,000 expansion of the company's laboratories in Detroit. The new program will be devoted mainly to research in molybdenum catalysts for upgrading low octane gasolines; in the synthesis of new molybdenum chemicals; and in Moly-sulfide, a new lubricant.

The General Electric Co. has announced formation of the chemical and metallurgical division, which includes the former chemical division and the carbonyl department. Robert L. Gibson, who will make his headquarters in Pittsfield, Mass., has been appointed general manager of the new division. Under the reorganization arrangement, the former chemical division's four operating departments will remain unaffected; their general managers will continue to report to Mr. Gibson. The chemical and metallurgical division will be made up of five operating departments: carbonyl, plastics, silicone products, chemical materials, and laminated and insulating products.

Plans for a research laboratory devoted exclusively to industrial products have been announced by the DuPont Co.'s textile fibers department. To be known as the Industrial Products Research Laboratory, it will be located at Newport, Del., and will develop additional uses for available fibers as well as establish objectives for the development of new fibers to meet the demands of American industry. Approximately 40 persons will be assigned to the new laboratory.

Modern Pharmacy, bimonthly publication of Parke, Davis and Co., celebrates its golden anniversary with the September issue. The magazine is distributed to nearly 100,000 pharmacists and pharmacies in the United States, Canada, Puerto Rico, and the Philippines.

Gordon Dean, former chairman of the Atomic Energy Commission, has announced the formation of the Nuclear Science and Engineering Corp. Dean is

chairman of the board of directors of the new company, and Ronald A. Brightsen, who was previously associated with the atomic power division of the Westinghouse Electric Corp., is president. The American Metal Co., Ltd., and the Ketay Manufacturing Corp., with Lehman Bros., investment bankers, participated in the creation of the new enterprise. The firm, which has headquarters in Pittsburgh, will provide a variety of technical services to organizations engaged in nuclear power development and to industries interested in the application of radioactivity to industrial products and processes.

John A. MacCartney of Parke, Davis and Co. reported recently that America's pharmaceutical industry is spending approximately \$60 million a year for research.

Miscellaneous

The National Academy of Sciences-National Research Council has announced the availability of the 1952-53 *Report of the Committee on the Measurement of Geologic Time*.

The October issue of *The Scientific Monthly* features articles on "Superficial aspects of modern organic reefs," by Preston E. Cloud, Jr.; "Should fluorides be added to public water supplies?" by James H. Shaw; "The world's principal food plants," by Karl S. Quisenberry, this being the second article of a series on *Species that feed mankind*; "Radio and television," as mediums for education, by C. V. Newsom; seven papers comprising a group on the general topic, *The present state of operationalism*, by Henry Margenau, Gustav Bergmann, Carl G. Hempel, R. B. Lindsay, P. W. Bridgman, Raymond J. Seeger, and Adolph Grünbaum. The issue also contains 24 book reviews and 8 communications from W. D. Hambly, C. G. Abbot, P. A. M. Dirac, Ernest Hocking, and others.

A new 134-page report on the smog research program conducted by the Stanford Research Institute in Los Angeles County during the past 6 yr has been released jointly by S.R.I. and the Western Oil and Gas Association, sponsors of the research. The report indicates that the stagnant condition of the air over such a large metropolitan area as Los Angeles, with its many industrial, commercial, and domestic activities, allows time for the ordinarily harmless chemicals emitted to remain in intimate contact and to react with one another photochemically. Sunlight is also a critical factor in the production of "parent" substances responsible for smog conditions.

The Society for General Microbiology, England, has recently undergone some reorganization. This society was founded in 1945, and since 1947 has published through the Cambridge University Press the *Journal of General Microbiology* and a series of symposiums. It has approximately 1260 members and has estab-

lished a permanent office at the Institute of Biology, Tavistock House South, Tavistock Sq., London, WC 1. Inquiries regarding application for membership and payment of subscriptions should be made to this office. Other questions should be addressed to the appropriate officer of the society, and inquiries about the journal made to the Cambridge University Press. All matters regarding meetings are dealt with by the meetings' secretary, E. F. Gale, dept. of biochemistry, Cambridge University. Other officers are pres., H. J. Bunker; sec., K. E. Cooper, dept. of preventive medicine, Bristol University; and treas., R. Lovell. Editors of the journal are B. C. J. G. Knight and A. F. B. Standfast.

Speakers have been announced for the 1954-55 traveling lecture program, a joint activity of the Oak Ridge Institute of Nuclear Studies and Oak Ridge National Laboratory in cooperation with the Atomic Energy Commission. The ORINS university relations division has just issued a brochure that lists the speakers, their subjects, and gives instructions for requesting lectures. A copy of the brochure and other information on the program may be obtained from W. W. Grigorieff, Chairman, university relations division, ORINS, Oak Ridge, Tenn.

"Man measures the universe" is the theme of UNESCO's 4th traveling science exhibition which will have its first public showing in October in Brussels, Ghent, and Liège, Belgium. It has been prepared especially for display in the countries of Western Europe during 1955 and 1956. The exhibition stresses measurement of distances and dimensions as the basis of all science. In the 4 yr during which UNESCO exhibitions have been traveling about the world, they have been shown in 26 countries to approximately 1¼ million persons.

Necrology

Eugene M. Bacigalupi, 73, head of the physics department at the University of Santa Clara, Santa Clara, Calif., 26 Aug.; Max W. Ball, 68, geologist, petroleum engineer, and former chief of the oil and gas division of the Interior Department, Washington, D.C., 28 Aug.; Arthur Carpenter, 64, archeologist, explorer, roentgenologic and radiation scientist for the Army Medical Research Laboratory at Fort Knox, Ky., 17 July; Bascom H. Palmer, 64, eye specialist, surgeon, and past president of the Florida Council for the Blind, Miami, Fla., 2 Sept.; Glenn A. Shook, 72, professor of physics and astronomy at Wheaton College, Norton, Mass., 26 Aug.; Franklin R. Strayer, 89, former instructor in physics and chemistry at Cornell University, Ithaca, N.Y., 2 Sept.; Herbert C. Woolley, 73, psychiatrist and former head of the Philadelphia State Hospital, Philadelphia, Pa., 28 Aug.; Roderick B. Young, former associate director of research at the Ontario Hydro-Electric Commission, Toronto, Canada, 24 Aug.

Book Reviews

Introduction to Nuclear Engineering. Raymond L. Murray. Prentice-Hall, New York, 1954. xiii + 418 pp. Illus. \$7.

The present-day writer of a textbook on nuclear engineering is handicapped, at the outset, because what he writes is determined not only by what is relevant and to the point, but also by what has been declassified and by what parts of this highly compartmentalized art are familiar to him. To write a textbook on nuclear engineering in the face of such handicaps requires a great deal of courage. One cannot help but admire Murray for collecting so much declassified information in a single volume of 418 pages.

Introduction to Nuclear Engineering is an outgrowth of a course of lectures that the author has given during the past 3 years to undergraduate nuclear engineering students at North Carolina State College. The tone of the book consequently reflects the current philosophic viewpoint in American engineering education—that the aim of undergraduate engineering education is to produce a large number of fairly competent practitioners rather than a smaller number of extremely skilled ones. Thus, the book is largely descriptive rather than analytic. For example, in the chapter on the design of liquid-metal cooled natural uranium reactors, the fine details have to be glossed over, even though the success of an actual design calculation must depend on such details.

What a student who reads Murray's book learns is how the expert in the field goes about dealing with various aspects of nuclear engineering; he hardly becomes an expert himself. Within this over-all limitation this will prove to be a useful book. It touches upon the basic sciences—nuclear physics, metallurgy, and heat transfer—necessary for an understanding of reactors. There are chapters on the "unit operations" of nuclear engineering—shielding, waste disposal, radiation detection and control, and isotope separation. There is an appendix on reactor theory as well as chapters on neutron experiments and the use of isotopes. Of particular interest are the chapters on specific reactor designs—on the water boiler and on several solid-fuel uranium reactors—and there is a table that gives design data for many of the existing reactors.

The choice of pedagogic material in a field that has grown up in such an unusual way as nuclear energy is very much a reflection of the viewpoint of the author. There is little educational tradition to guide him. Murray's choice and therefore, by implication, his definition of nuclear engineering can hardly be criticized. I would have liked a chapter on nuclear engineering gadgetry—canned rotor pumps, remote handling equipment, and the like—and in general, greater emphasis on the chemical aspects of nuclear reactors.

On the whole, the organization of the material is adequate. The chapters on specific reactor design are

placed, somewhat oddly, in the middle of the book rather than after all the unit operations have been covered. This means that reactor design is conceived mainly as including reactor statics, choice of materials, and heat transfer. Such aspects of design as control and shielding are not included in the reactor-design chapters.

Nevertheless, the chapters on reactor design are illuminating, especially since they are the first accounts to appear in the open literature of how the conflicting design requirements imposed by considerations of heat transfer, nuclear physics, and materials limitations are resolved in a practical design. If the book were classified, the author could have indicated in greater detail how well the methods of design really work. As it is, the reader must be left with a slightly uneasy feeling that the chosen examples always come out "just right."

The book is written with a fair degree of authority. The most significant misstatement that I noticed is in the discussion of the temperature effect in natural-uranium reactors. The temperature effect on the resonance capture in a natural-uranium reactor is, contrary to the statement in the book, hardly affected by the neutron temperature; it is almost entirely determined by the fuel temperature.

Writing a textbook on nuclear engineering under present-day handicaps is an extraordinarily difficult task. Although Murray's book cannot be considered definitive, even in terms of what it is intended to be, an elementary textbook, it nevertheless contains much interesting material and ought to prove to be a useful introduction to nuclear engineering.

ALVIN M. WEINBERG

Oak Ridge National Laboratory

Principles of General Ecology. Angus M. Woodbury. Blakiston, New York, 1954. viii + 503 pp. Illus. \$6.

This is the third American textbook on ecology to appear in 5 years, but in some ways it appears to antedate its successors. While here and there traces of recent thought are evident, the statement in the introduction that the "eco-system approach . . . is used by some geographers and is the one utilized in this work" is on the whole unfulfilled. The book follows the conventional pattern of organization: part I, "General considerations"; part II, "The physical environment" (7 chapters, on soils, water, radiant energy, gravity and periodicities, climate, and physical adaptations); and part III, "Biotic interrelationships" (16 chapters).

The emphasis is on upland terrestrial ecology (indeed, it has been facetiously described as the "ecology of Utah"). Most of the statements about conditions in the ocean are misleading when they are not erroneous, and, although this might be forgiven on the ground

that this book will obviously be used in regions far from the sea, another way of looking at it is to remember that the students will not be able to realize this, inasmuch as the author has stated in at least two places that such a book as this is supposed to provide a background in ecology for oceanography as well as for many other fields. Even closer to home, as far as the book itself is concerned, is the paucity of material concerning fresh-water environments. A lake is simply a wide place in a stream, and streams are mentioned much less frequently than Great Salt Lake. (The diagram of "important habitat types in North America" on page 48 omits streams entirely). On the other hand, the terrestrial aspects are well covered; the chapters on soil and climate are outstanding; and those on populations, geographic distribution, and the like are good workman-like jobs. There are many interesting illustrations, especially photographs of scenes in Utah, but the reiterated tree of life, modified to suit the discussion (in one place there are six versions of it in a row), becomes tiresome.

It might be best if those who decide to use this book think of it as "Principles of Terrestrial Ecology," and refer to a limnology textbook to fill out the details that they may need to understand that aspect of the transmontane environment, which is otherwise treated in such detail. Conversely, aquatic ecologists will find this a useful summary of matters unfamiliar to them.

JOEL W. HEDGPETH

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The Origins of Psycho-Analysis. Letters to Wilhelm Fliess, drafts and notes: 1887-1902. Sigmund Freud. Marie Bonaparte, Anna Freud, and Ernst Kris, Eds. Trans. by Eric Mosbacher and James Strachey. Basic Books, New York, 1954. xi + 486 pp. \$6.75.

The student and practitioner of psychoanalysis is provided with an opportunity to look behind the scenes and to get a fascinating intimate glimpse into the background of personalities and circumstances that led to its development. Skillful footnotes and introduction by Kris tie the content of the letters together and permit the reader to link thoughts and formulations with the corresponding well-known literature.

The less biased reader will also be impressed by the brilliant creativity of Freud's mind, but he cannot fail to notice the precarious scientific ground on which the whole edifice of psychoanalysis seems to be built.

When Breuer, who had introduced him to a new method of therapy, could not follow Freud's emphasis on sexuality in the etiology of the neuroses, Freud turned to the only contemporary who, like him, had accepted a pan-sexual theory of neurosis. Fliess became his "only audience," the two men uniting and fortifying each other against the rest of the scientific world. Kris does not see the attraction of the two men for each other as being based on their preoccupation with sex and on the similarity of their personalities.

Both are visionaries (in Freud's own words, p. 130). Both are fond of far-reaching speculations. Fliess is criticized by Kris for working on his theories "with an obstinacy and a lack of objectivity which ignored all inconsistencies and inconveniences" (p. 8), while Freud is praised for the "consistency which holds his objective in mind in spite of all difficulties and contradictions" (p. 26).

The critical reviewer of Freud's writings has always wondered how Freud could use "free association" as a method of investigation, not recognizing it merely as a method of therapy. This volume explains why the fallacious findings of his approach, leading twice to a near personal and scientific collapse in 1897 and 1900 (letters 69 and 130), did not stop Freud from continuing with the same clinical procedure. He developed his ideas first and then sought the clinical evidence, thus imposing his ideas upon his patients, as Fliess discovered after 15 years of closest friendship and collaboration (pp. 40, 344). The technique is little mentioned in the published letters, except in one "Draft J." Here the method of putting pressure upon the patient until his mind yields what Freud expects to find is clearly described.

Freud waited for his inner voice to reveal to him the deepest secrets of the human mind, a process that Kris calls a "surge forward from the preconscious" (p. 307), which "worked over scientific connections before they became conscious" (p. 230). This tendency to gain scientific insight from within himself was accentuated when Freud decided to get at the roots of his scientific errors by analyzing himself and his dreams—a curious way of scientific investigation, indeed.

The intimate revelations provided by this volume about the origins of psychoanalysis may facilitate the recognition of the pattern behind the unrealistic constructs of psychoanalysis.

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Economic Geography. Clarence Fielden Jones and Gordon Gerald Darkenwald. Macmillan, New York, rev. ed., 1954. xxv + 612 pp. Illus. \$6.75.

Would you like to know about iron ore production by states and its movement to smelters? Or are you interested in rubber output in Malaya and Liberia? Clarence Jones and Gordon Darkenwald have provided 612 pages of encyclopedic yet meaningful data on man's utilization of the earth, illustrated by 442 maps and photographs.

Geographers divide their subject into three broad categories: systematic, regional, and techniques such as cartography. Within the field of systematic geography the main divisions are economic, social, and political. Each considers the distributional aspects of human affairs. *Economic Geography* is organized along occupational lines, and is thus an evaluation of hunting and fishing, forest industries, grazing industries, agriculture in its many aspects, mining, manufacturing, transportation, and trade.

This is the second edition of this standard textbook, which originally appeared in 1941. The revision is extensive, and the book will be welcomed by teachers, students, and the general reader. The book opens with a reminder that "some regions offer a choice of only a few occupations, whereas others offer a choice of many," and closes with the following paragraph.

The United States is intricately associated in a complex of trade relations that ties us commercially to nearly every region of the world. Prosperous farmers require a market for their surplus products; successful industries rely, not only on foreign markets for surplus manufactured articles, but also on foreign sources for certain industrial raw materials. Our high standard of living depends on the variety and quantity of goods we consume. To maintain this standard we must utilize such articles as rubber, tin, hemp, vanadium, bauxite, asbestos, sugar, coffee, and spices; none of these is produced in sufficient quantities in the United States. If our foreign commerce were stopped, we would be without such things as automobiles, electricity, telephones, daily newspapers, coffee, airplanes, and streamlined trains—things that are a vital part of our high standard of living. Thus we must arrange to exchange goods with peoples who produce the things we need; we must also arrange to dispose of our own surplus products to those who can use them. The successful adjustment of the problems involved in making these arrangements depends on an adequate understanding of our own occupations and those of other peoples. This is the chief purpose of the study of economic geography. It is basic to the understanding and solution of international problems, whether they be economic, political, or social.

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New Books

- The Elementary Chemical Composition of Marine Organisms.** Memoir No. 2. A. P. Vinogradov. Trans. by Julia Efron and Jane K. Setlow. Sears Foundation, Yale Univ., New Haven, 1953. xiv + 647 pp. \$17.
- A Monograph of the Fungus Genus *Cercospora*.** Charles Chupp. Charles Chupp, Ithaca, N.Y., 1954. 667 pp. Illus. \$10.
- Infinite Abelian Groups.** Irving Kaplansky. Univ. of Michigan Press, Ann Arbor, 1954. v + 91 pp. Paper, \$2.
- Advances in Genetics.** vol. VI. M. Demerec, Ed. Academic Press, New York, 1954. ix + 488 pp. Illus. \$9.80.
- Petroleum Microbiology.** An introduction to microbiological petroleum engineering. Ernest Beerstecher, Jr. Elsevier Press, Houston, 1954. xv + 375 pp. Illus. \$8.
- Psychomotor Aspects of Mental Disease.** An experimental study. H. E. King. Harvard Univ. Press, Cambridge, Mass., 1954 (For the Commonwealth Fund). xiv + 185 pp. Illus. \$3.50.
- Biological Effects of External Radiation.** Henry A. Blair, Ed. McGraw-Hill, New York-London, 1954. xvii + 508 pp. Illus. \$7.
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- Contributions to Science, No. 2.** Florida State Univ. Studies, No. 13. Weymouth T. Jordan, Ed. Florida State Univ., Tallahassee, 1954. 100 pp. Illus. + plate.
- Proceedings of the Eighth Annual Session of the Ceylon Association for the Advancement of Science** (27-29 Nov. 1952). pt. 1, Sectional programs, abstracts. The Association, Univ. of Ceylon, Colombo, 1952. 39 pp.
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(Continued on page 11A.)

Technical Papers

Effect of Some Steroid Compounds on Ovine Rumen Function

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An implant of stilbestrol has been shown to increase the rate of gain and feed efficiency in lambs (1-4). Tests were designed to determine whether stilbestrol, cholesterol, or estrone would influence the digestion of cellulose by rumen microorganisms *in vitro* and to determine the effect of stilbestrol on the digestion of cellulose and crude protein by sheep.

Studies were made using the artificial rumen techniques described by Brooks (5). Stilbestrol was tested at levels of 2, 8, 10, 16, and 20 μ g per artificial rumen, and estrone and cholesterol were each tested at the 20- μ g levels. One microgram was equal to 1 ppm dry matter. Each artificial rumen contained 500 mg of cellulose and was paired with one containing the same ingredients other than the substances under test.

The effects of stilbestrol, estrone, and cholesterol on cellulose digestion in the artificial rumen are shown in Table 1. When stilbestrol was added at low levels (2 and 8 μ g) in trial 1, there was a slight but nonsignificant increase in cellulose digestion. The addition of stilbestrol (16 μ g in trial 1, or 10 and 20 μ g in trial 2) increased cellulose digestion ($P < 0.05$). Twenty microgram of estrone increased cellulose digestion 63 percent ($P < 0.01$), and 20 μ g of cholesterol increased it 35 percent ($P < 0.05$). The differences between cellulose digestion in rumina containing 20 μ g of stilbestrol, estrone, and cholesterol were not significant.

The *in vivo* effect of stilbestrol on cellulose and

Table 1. Effect of some steroid compounds on cellulose digestion by ovine rumen microorganisms *in vitro*.

Trial	Mixture fermented	No. of rumina	Avg. cellulose digestion (%)
1	Basal ration	6	35.1
1	Basal ration + 2 μ g stilbestrol	6	36.6
1	Basal ration + 8 μ g stilbestrol	6	37.6
1	Basal ration + 16 μ g stilbestrol	6	49.1*
2	Basal ration	10	36.7
2	Basal ration + 10 μ g stilbestrol	10	44.7†
2	Basal ration + 20 μ g stilbestrol	5	51.4*
2	Basal ration + 20 μ g estrone	5	57.3†
2	Basal ration + 20 μ g cholesterol	5	48.4*

* Difference in cellulose digestion (experimental vs. basal) significant ($P < 0.05$).

† Difference in cellulose digestion (experimental vs. basal) highly significant ($P < 0.01$).

protein digestion was studied in three lots of 5 crossbred yearling wethers. The basal ration provided 908 g cottonseed hulls, 95 g casein, 6 g Cr_2O_3 , and 2500 IU vitamin A per sheep daily. The sheep had free access to salt and a mineral mixture of equal parts dicalcium phosphate, calcium carbonate, and sodium chloride containing 2 oz of cobalt sulfate per 100 lb of mixture. A 14-day preliminary period was followed by a 4-day collection period. The digestion trials and chemical determinations were conducted as described by Brooks *et al.* (6).

As is indicated in Table 2, the coefficient of digestibility of cellulose was increased 16 percent ($P < 0.05$), and the coefficient of digestibility of protein was increased 18 percent in animals that received 10 or 20 mg of stilbestrol per day. The differences in the coefficients of digestibility of cellulose between the basal lot and the stilbestrol-fed lots were significant ($P < 0.02$). The differences between the coefficients of digestibility of crude protein approach significance.

Table 2. Effect of stilbestrol on the coefficients of digestibility of cellulose and protein in sheep.

Lot no.	Ration	Coefficients of digestibility	
		Cellulose	Crude protein
1	Basal	41.9	37.5
2	Basal + 10 mg stilbestrol per sheep per day	47.9	43.2
3	Basal + 20 mg stilbestrol per sheep per day	48.7	44.7

In a subsequent test, lot 3 sheep continued to receive 20 mg of stilbestrol per head daily. Two of them developed anorexia during the first week and appeared listless. An edematous swelling appeared around the anus of one sheep. Contractions of the abdominal muscles accompanied by apparent pain were observed 24 hr after the first symptoms had appeared. Digital examination indicated that the muscle tonus of the lower intestine was reduced and that the urethra and prostate had enlarged. Similar conditions have been described in Australia where sheep were pastured on swards high in subterranean clover (7). When the sheep was taken off the stilbestrol ration and given a subcutaneous injection of 100 mg of testosterone, it made a rapid recovery. Other sheep receiving stilbestrol showed mild symptoms similar to those seen in the sheep that was treated and were taken off the experiment.

Summary. (i) Stilbestrol (10 or 20 ppm) increased cellulose digestion by ovine rumen microorganisms *in vitro* and *in vivo* but could not be tolerated by wethers at these high levels. (ii) Cholesterol and estrone in-

creased cellulose digestion by rumen microorganisms *in vitro* (8).

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3 May 1954.

Particle Size and Shape of Purified Tomato-Ringspot Virus

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The particle size of the tomato-ringspot virus has been estimated at 50 m μ or less according to ultra-filtration techniques (1). The shape of such particles has not been described insofar as we are aware. Therefore, investigations were undertaken to determine the particle size with more precision and to ascertain its shape.

Purification of the virus. Tobacco plants of the Holmes' necrotic type with three or more fully developed leaves were inoculated with tomato-ringspot virus obtained from W. C. Price. Leaves showing typical symptoms after 18 days' incubation were frozen, minced, and extracted with dipotassium phosphate. The extract was then clarified by low-speed centrifugation. Initial concentration and purification were achieved by differential centrifugation in the preparative centrifuge, Spinco, Model L (2). The resultant pellets from both diseased and healthy tissues were suspended in 0.01M potassium phosphate buffer (pH 7) for each run. The pellet from the final centrifugation was resuspended in 0.1 ionic strength phosphate buffer (pH 6.5) for use in electrophoresis. Final purification was attained by electrophoresis for 312 min in the Tiselius apparatus.

Electron microscopy. Specimens for the electron microscope were prepared by the protein monolayer technique (3). This procedure involves the application of a suspension of virus particles in a dilute protein solution to a point on an aqueous surface. The protein spreads spontaneously and forms an insoluble monolayer in which the particles to be examined are uniformly distributed. The monolayer with its imbedded particles is then transferred to a celloidin-

covered screen and shadowed with 8 A of uranium at a grazing angle of 16°. The magnification of an RCA-type EMU microscope was calibrated by a replica of a precision-ruled grating, consisting of 15,000 lines/in., manufactured by the Ford Company.

Particle size and shape. Preparations from the infected and virus-free tissue were examined with the electron microscope for differences in particle size and shape. Electron micrographs (Fig. 1) of preparations of an infective fraction from the electrophoresis apparatus indicate the presence of four- to six-sided particles having a cross section of 43 m μ when measured perpendicularly to the direction of the shadowing. The depth of the particle as obtained from shadow measurements was 13.5 m μ . Thus, the particles resemble flattened cylinders or pills. It is to be recognized that the measurement of shadows cast by individual particles is subject to uncertainty owing to local shadow angles, to the difficulty of making a precise determination of filament position, and to other factors. However, if it is assumed that this virus is not rigid and that the monolayer technique permits the distortion of the shape, then, from the dimensions given here, the volume may be equated to that of a sphere, in which case a diameter of 27 m μ is obtained.

Electron micrographs of preparations from virus-free plants contained many spheroidal particles approximately 14 m μ in diameter and much amorphous material. These particles were not observed in the electrophoretic fraction of extracts from virus-infected plants used for electron microscopy, but they were present in two of four other fractions. The polyhedral particles observed in infected tissue extracts as described in the preceding paragraph were not found in preparations from virus-free plants.

Infectivity. Aliquots of preparations from virus-infected plants containing the polyhedral particles were

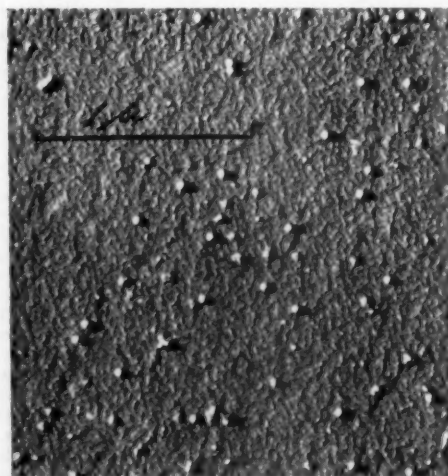


Fig. 1. Electron micrograph of particles from purified tomato-ringspot virus preparations ($\times 33,000$).

highly infective as determined by bioassay on primary cowpea leaves (*Vigna sinensis* Endl. var. Wilt Resistant), whereas those from uninoculated tobacco plants showed no virus activity.

Comparison with tobacco-ringspot virus. The tomato-ringspot and tobacco-ringspot viruses have similar host ranges (4), but the two viruses may be differentiated by cross-immunity tests and serologic reactions (5). It is apparent from the results reported here that the viruses may also be differentiated on the basis of particle size and shape. The tobacco-ringspot virus has been shown previously (2) to have an average particle diameter of 20.9 and 22 mμ, depending on the direction of measurement, and a polyhedral shape that approximates a sphere. On the other hand, the diameters of the tomato-ringspot virus were 43 and 13.5 mμ, with a polyhedral shape that resembles a flattened cylinder or pill.

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22 April 1954.

Rickettsial-Interference Phenomenon: A New Protective Mechanism

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Previous studies from this laboratory have shown that under certain experimental conditions an interference phenomenon exists between certain rickettsial agents in guinea pigs (1). The data presented in this report (2) indicate that the rickettsial-interference phenomenon (RIP) is not due to competition between the rickettsiae for the same susceptible host cells. The isolation of a component from *Rickettsia rickettsii* is described that interferes with a challenge dose of a virulent strain of *Rickettsia rickettsii*.

Quantitative studies on the number of susceptible cells infected during the rickettsial-interference phenomenon. It has been shown that under certain conditions a low virulent T-type strain of *R. rickettsii* will protect guinea pigs against a highly virulent R-type strain of *R. rickettsii* (1). Further experiments were carried out to see whether this protection could be due to competition for the same susceptible host cells. Rickettsiae of a highly virulent R-type were purified from infected yolk sacs by the celite and albumin method of Bovarnick and Miller (3), and then counted under the electron microscope (4). The purified suspension was then inactivated by ultraviolet

light. Various dilutions of this suspension were then injected intraperitoneally into guinea pigs, 15 animals being used for each dilution. After 3 hr, various numbers of living, highly virulent R-type strain of rickettsiae were injected intraperitoneally into the guinea pigs. This latter suspension was prepared and counted in the same way as the first suspension. Suitable controls were included in all experiments.

Three such experiments were carried out, all of them giving similar results. A typical experiment is shown in Table 1. It can be readily seen that the protection seems to be dependent on the ratio of interfering dose to infecting dose and not on the number of susceptible host cells.

It should be emphasized that there was little, if any, reactivation of the ultraviolet-treated organisms in the guinea pigs. This was shown by the fact that none of the guinea pigs receiving the treated rickettsiae showed any fever, and it takes only 100 living R-type strain organisms to produce 6 days of fever and even serotal reactions in some of the animals, as is shown in Table 1. Furthermore, guinea pigs injected with 1×10^{11} ultraviolet-inactivated rickettsiae were sacrificed at 2-day intervals for a period of 12 days, and their various organs were titrated in chick embryos (4). No viable rickettsiae could be demonstrated by this method, which is sensitive enough to detect at least 10 viable rickettsiae of the R-type strain (4). Injections of 1×10^6 ultraviolet-inactivated rickettsiae gave no protection even when the challenge dose was only 100 living virulent rickettsiae. If the living virulent organisms were given 3 hr before the inactivated rickettsiae, little, if any, protection was observed with any of the ratios shown in Table 1.

If the routes of inoculation of a low-virulent and of a high-virulent strain of *R. rickettsii* were changed,

Table 1. Effect of varying the number of rickettsiae on the interference phenomenon.

No. of killed R-strain organ- isms injected	No. of living virulent R-strain organ- isms injected	Average days of fever	Serotal reac- tion*	Fatal- ity*
None	1×10^2	6.4 ± 0.92	5/15	2/15
1×10^7	1×10^4	2.0 ± 0.82	2/15	0/15
1×10^7	None	0	0/15	0/15
None	1×10^4	6.1 ± 1.1	11/15	4/15
1×10^7	1×10^2	8.1 ± 1.3	9/15	11/15
None	1×10^2	7.6 ± 1.2	11/15	15/15
1×10^6	1×10^2	2.1 ± 0.85	2/15	0/15
1×10^6	None	0	0/15	0/15
1×10^6	1×10^{10}	8.1 ± 1.3	13/15	12/15
None	1×10^{10}	8.3 ± 1.1	14/15	15/15
1×10^{11}	1×10^{10}	2.3 ± 0.81	2/15	1/15
1×10^{11}	None	0	0/15	0/15

* The numerator indicates the number of animals showing serotal reaction or dying of spotted fever.

Table 2. Effects of challenging guinea pigs by different routes.*

Route of inoculation of low-virulent U-type strain (300,000 egg LD ₅₀)†	Route of inoculation of high-virulent R-type strain (3000 egg LD ₅₀)‡	Average days of fever	Average height of fever	Scrotal reaction‡
Intraperitoneal	Intraperitoneal	1.9 ± 0.88	39.9 ± 0.11	1/15
	Intraperitoneal	8.1 ± 1.2	40.6 ± .12	12/15
Intraperitoneal	Intramuscular	3.4 ± 0.86	40.0 ± .13	0/15
	Intramuscular	5.0 ± 0.76	40.5 ± .11	2/15
Intraperitoneal	Intracardial	5.1 ± 0.98	40.4 ± .12	3/15
	Intracardial	7.6 ± 1.1	40.6 ± .09	5/15
Intramuscular§	Intramuscular	1.9 ± 0.79	40.2 ± .14	0/15
	Intramuscular	4.8 ± 0.86	40.4 ± .12	2/15
Intramuscular	Intraperitoneal	1.8 ± 0.72	40.0 ± .12	1/15
	Intraperitoneal	7.3 ± 1.1	40.6 ± .07	10/15
Intramuscular	Intracardial	3.6 ± 0.92	40.3 ± .13	1/15
	Intracardial	8.1 ± 1.2	40.5 ± .11	5/15
Intracardial	Intracardial	4.4 ± 1.2	40.4 ± .13	3/15
	Intracardial	8.8 ± 1.3	40.6 ± .11	6/15
Intracardial	Intraperitoneal	1.0 ± 0.51	39.9 ± .14	1/15
	Intraperitoneal	7.5 ± 1.0	40.6 ± .14	11/15
Intracardial	Intramuscular	0.9 ± .63	40.0 ± .13	0/15
	Intramuscular	4.1 ± 1.2	40.4 ± .09	2/15

* All injections were in 0.2-ml amounts. The U-type strain by itself shows no detectable symptoms in guinea pigs.

† One egg LD₅₀ of either the U-type strain or the R-type strain is equal to about 20 to 100 organisms (4).

‡ The numerator indicates the number of animals developing scrotal reaction.

§ Intramuscular injections were all in the hind leg and in this case both injections were in the same hind leg.

the results shown in Table 2 were obtained. Doses of 300,000 egg LD₅₀ of a low-virulent U-type strain of *R. rickettsii* (4) and doses of 3000 egg LD₅₀ of a virulent R-type strain were used. The virulent strain was injected 4 hr after the low-virulent strain. This experiment was repeated four times with similar results.

Isolation of a component from rickettsiae that will interfere with virulent rickettsiae. An R-type strain of *R. rickettsii* was isolated from yolk sacs and purified by the celite and albumin procedure. It was then treated in a sonic vibrator for 30 min. After treatment, the suspension was centrifuged for 1 hr at 30,000 *g* and at 5°C. The supernatant fluid was collected; it was found to protect between 80 and 90 percent of the guinea pigs against a challenge of the virulent R-type strain. The R-type strain was given 3 hr after injection of the supernatant material. The supernatant fluid by itself caused no detectable symptoms in the guinea pigs. If a purified suspension was centrifuged for 1 hr at 30,000 *g* and at 5°C without being treated with sonic vibration, the supernatant fluid from such a suspension exhibited no interference effect and caused no symptoms.

These experiments, together with microscopic examination of such preparations and electron microscope pictures, have strongly indicated that the interfering effect of such preparations is not due to whole rickettsiae that might be present. About 30 percent

of the rickettsial-interfering activity is recovered in these preparations. If this activity were due to whole rickettsiae, they should have been readily seen by the methods that were used. Concentrated preparations of the soluble antigen of *R. rickettsii* had no ability to interfere with the virulent rickettsiae.

The best preparations prepared by various fractionation procedures contained protein, lipid, carbohydrate, less than 0.1 percent of phosphorus, no pentosenucleic acid, and no desoxyribosenucleic acid.

Discussion. Any hypothesis to explain the rickettsial-interference phenomenon must account for these experimental facts: (i) Protection is dependent upon the ratio of interfering dose to the challenge dose but not upon the number of susceptible host cells. (ii) Mobilization and phagocytic activity of white cells, an inflammatory response, antibody formation, or the reversal of the protective effect by multiple infection of single cells by living virulent organisms do not play a major role in this phenomenon (1, 5). (iii) The challenge organisms are distributed in the same organs and tissues and to the same extent in both susceptible animals and animals where the interference phenomenon occurs, but there is much less multiplication of the challenge dose in the latter case (1, 5).

The relation of the RIP to the virus-interference phenomenon reported in experimentally inoculated animals is not clear. However, it should be pointed

out that the competitive "cell for cell" theory used to explain the virus-interference phenomenon has not been rigorously proved to occur in experimentally infected animals, since this explanation is based on bacterial-virus systems and the chick embryo-influenza system. Experiments are in progress to determine whether certain animal virus-interference systems are actually due to competition for susceptible host cells between two viruses.

Note added in proof: The RIP is highly specific under the experimental conditions shown in Table 1, nine bacterial species and nine viruses being tried as well as various other substances. All gave no interference. The RIP is also independent of the time that the challenge dose is given, provided that it is after the protective dose but not longer than about 10 days after the protective dose (1).

Recent results in animals, using a neurotropic virus system, have strongly indicated that in this case interference cannot be due to a saturation of susceptible cells by the protective dose. These results so far are very similar to those described here for the RIP.

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29 July 1954.

Potassium and Sodium Balance in Mammalian Red Cells

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Estimations performed by flame spectrophotometry (1) of the red cell potassium and sodium content for nine mammals (man, baboon, rabbit, rat, horse, sheep,

ox, cat, and dog) showed considerable species variation, whereas the chloride and calculated bicarbonate values were more constant (Table 1). The results confirm values by chemical methods for some species previously reported (2, 3). The individual red cell: plasma concentration ratios ranged from 1.5 to 32 for potassium and 0.1 to 0.9 for sodium; the red cell: plasma chloride and bicarbonate ratios were 1.2 to 1.6. The mechanism of distribution of potassium and sodium is, therefore, different from that of chloride or bicarbonate.

Blood specimens from the various species were collected in tubes containing heparin powder of low sodium content and were spun immediately under oil; the supernatant plasma, buffy coat, and superficial red cells were removed within 15 min of sampling to control cell-plasma ion and fluid exchange. The packed red cells were resuspended in an equal volume of:

- 1) One-percent NaCl-glucose-phosphate buffer, pH 7.6, at room temperature; a steady state with minimal electrolyte variation and normal glycolysis occurred for 6 to 12 hr (1).
- 2) Buffer with or without glucose and refrigerated at 2° to 7°C for 3 to 7 days; glycolysis was minimal; in accord with chemical concentration gradients, potassium diffused out and slightly more sodium in, with resultant cell swelling (Table 2a).
- 3) Cells from the refrigerated buffer were resuspended in isotonic saline-glucose-potassium, 5 milliequivalents per liter phosphate buffer solutions (pH, 6.8-8.0), in volume equivalent to that removed, and incubated at 37°C for 6 to 8 hr; restoration of glycolysis was associated with sodium extrusion slightly greater than potassium influx, with correction of cell volume and content (Tables 2b and 3).

Samples were removed periodically for potassium, sodium, and chloride estimations in the whole suspension and fluid medium, with calculation of the red cell values from determination of the red cell water and the packed cell volume corrected for trapped intercellular fluid (1). The hematocrit values were used to calculate water shifts in the system.

From chloride values and pH determinations of the fluid medium and red cell hemolysate, a Donnan ratio, r , $[Cl^-]_e/[Cl^-]_i = [H^+]_i/[H^+]_e$, calculated in log

Table 1. Ionic patterns of mammalian red cells; mean values. The notations $[K]$, . . . denote milliequivalents per liter of red cell or plasma water.

Species and No: estimated	Red cells			Plasma			Ratios		
	[K]	[Na]	[Cl]	[K]	[Na]	[Cl]	$\frac{[K]_i}{[K]_e}$	$\frac{[Na]_i}{[Na]_e}$	$\frac{[Cl]_i}{[Cl]_e}$
Man (120)	136	19	78	5.0	155	112	27.4	0.16	1.44
Baboon (56)	145	24	78	4.7	157	115	30.8	.15	1.48
Rabbit (15)	142	22	80	5.5	150	110	25.4	.15	1.38
Rat (36)	135	28	82	5.9	152	118	23.0	.18	1.44
Horse (8)	140	16	85	5.2	152	108	25.0	.11	1.27
Sheep (18)	46	98	78	4.8	160	116	9.6	.61	1.49
Ox (28)	35	104	85	5.1	150	109	6.8	.69	1.28
Cat (5)	8	142	84	4.6	158	112	1.7	.90	1.33
Dog (28)	10	135	87	4.8	153	112	2.1	.88	1.44

Table 2. Concentration ratios in human red cells (a) refrigerated for 6 days, followed by (b) reincubation with glucose at pH 7.6 for 8 hr.

Hours	(a) 4°C				(b) 37°C	
	0	48	96	144	4	8
pH, fluid medium	7.35	7.20	7.25	7.25	7.50	7.40
pH, cells	7.20	7.10	7.10	7.15	7.35	7.25
Hematocrit	48.4	50.2	52.8	54.6	52.8	49.2
$[K]_i/[K]_o$	130	18	12	7	14	25
$[Na]_i/[Na]_o$	0.12	0.30	0.38	0.42	0.28	0.17
$[Cl]_i/[Cl]_o$	1.4	1.3	1.3	1.2	1.3	1.4
$\log [H]_i/[H]_o$	0.15	0.10	0.15	0.10	0.15	0.15
$\log [Cl]_i/[Cl]_o$.14	.11	.12	.08	.11	.14

$[K]_i$, . . . denote concentration of red cell ion, milliequivalent per liter of cell water.
 $[K]_o$, . . . denote concentration of suspension ion, milliequivalent per liter of water.

Table 3. Incubation of refrigerated human red cells with glucose and at different pH values for 8 hr at 37°C.

Initial pH, fluid	6.80	7.00	7.20	7.40	7.60	8.00
Final pH, fluid	6.70	6.95	7.10	7.30	7.40	7.70
Final pH, cells	6.70	6.90	7.00	7.15	7.25	7.50
$[K]_i/[K]_o$	19	21	22	25	25	27
$[Na]_i/[Na]_o$	0.25	0.25	0.20	0.16	0.17	0.15
$[Cl]_i/[Cl]_o$	1.1	1.2	1.3	1.4	1.4	1.6
$\log [H]_i/[H]_o$	0	0.05	0.10	0.15	0.15	0.20
$\log [Cl]_i/[Cl]_o$.04	.08	.11	.16	.14	.20
Glucose utilization, mg/lit red cells per hour	165	190	230	250	280	295

form, obtained with high correlation. The bicarbonate and pH ratios, calculated from gas estimations on some samples by the method of Yeomans and Stueck (4), showed fair correspondence. Hence, the distribution of chloride, bicarbonate, and hydrogen ions in mammalian red cells accords with simple diffusion. The results for human red cells are presented in Tables 2 and 3. The Donnan ratio for chloride ranged from 1.5-1.7 at pH 7.7 to 1.0-1.1 at pH 6.7 and was independent of the metabolic status of the red cells. The high cell chloride at low pH resulted only from the reduced buffering capacity of the nondiffusible cell hemoglobin (isoelectric point, pH 6.6-6.8) and organic phosphate. Harris and Maizels (5) report that human red cells, refrigerated for 4 to 8 wk, show chloride and cation ratios approaching 1, that is, diffusion equilibrium.

The potassium and sodium ratios were dependent on the degree of cell glycolysis (Tables 2 and 3). With decreasing pH, some inhibition of glycolysis occurred at 37°C with diminished sodium extrusion and potassium uptake by red cells (Table 3). The extrusion of sodium is an active process (6). Apart from the dog and cat red cell, the simultaneous influx of potassium is either carrier conditioned or an active process requiring energy (7). It does not conform to the criteria given by Ussing (8) for passive or exchange diffusion. The electric potential of the Donnan ratio is about 10 to 15 mv and could not produce more than a twofold concentration ratio between red cells and plasma. Since the red cell in heparinized plasma is almost a perfect osmometer (3, 9) and ^{42}K exchanges

completely by a single rate constant (10, 11), it is improbable that sufficient potassium could exist in bound form to account for potassium accumulation by diffusion.

Thus, the process of potassium accumulation in red cells contrasts with the diffusion process in nerve and muscle (12). Here, high intracellular nondiffusible anions (proteins, organic phosphates, and so forth) and low chloride yield $[Cl]_i/[Cl]_o$ and $[K]_i/[K]_o$ ratios of 20 : 1 or greater with resting electric potentials of 50 to 100 mv. This negative force provides steep electrochemical gradients for the passive exchange diffusion of positive potassium ions following active sodium extrusion.

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2 June 1954

Studies on the Plasma Proteins in the Interstitial Fluid of Muscle

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It has been shown that the total extravascular mass of preformed plasma proteins is approximately equal to the mass of plasma proteins within the vascular system (1-6). It has also been shown that these proteins in the extravascular pool are in dynamic equilibrium with those in the intravascular compartment (7). In studies of their distribution in human tissues, it was demonstrated by qualitative methods that various plasma proteins could be found in connective tissue and, to a lesser extent, in the cells of many organs (8). The present investigation (9) was undertaken in an attempt to determine the actual concentration of the plasma protein present in the interstitial fluid of muscle.

Experimental procedure. Rabbits weighing about 2 kg were employed in this study. A given plasma protein was injected into the marginal ear vein, and 48 hr later, when this protein had equilibrated between the extravascular and intravascular compartments as shown by its exponential rate of fall (4), a second protein was injected into the marginal vein of the opposite ear. Fifteen minutes after injection of the second protein, the animal was exsanguinated from the heart, and a muscle sample was immediately taken from the anterior aspect of each thigh. In one instance, No. 817, three samples were taken and treated separately, one from each anterior thigh and a third from the posterolateral aspect of the right thigh.

The muscle samples were weighed rapidly and homogenized in cold saline in a Waring Blender for a period of 1 min. A third protein was added to the muscle homogenates and mixed thoroughly. After storage at 2°C for 24 hr, the homogenates were centrifuged at 5000 *g* for 1 hr; the resulting supernates were centrifuged at 5000 *g* for 1 hr and then at 24,000 *g* for another hour. The resulting muscle extracts were analyzed for the three proteins employed, and the serums were analyzed for the two proteins that had been injected into the rabbit.

Calculations. Let *A* represent the protein given intravenously and allowed to equilibrate between the extravascular and intravascular compartments for 48 hr, let *B* represent the protein given 15 min before exsanguination, and let *C* denote the protein added to the muscle homogenate; *A_s* and *B_s* are the concentrations of *A* and *B* in serum; *A_m*, *B_m*, and *C_m* are the concentrations of the three proteins in the muscle extract; and *A_e*, *B_e*, and *C_e* are the total amounts of these proteins in the muscle sample. If *V_m* is the volume of distribution of proteins *A*, *B*, and *C* in the muscle homogenate, since *C_e* is known, then:

$$V_m = C_e / C_m \quad (1)$$

and

$$A_e = V_m A_m, B_e = V_m B_m. \quad (2)$$

If *S_e* is the apparent volume of serum left in the muscle sample,

$$S_e = B_e / B_s. \quad (3)$$

If *A_i* and *A_e* represent the intravascular and extravascular amounts of *A*, respectively,

$$A_i = S_e A_s, \quad (4)$$

$$A_e = A_e - A_i. \quad (5)$$

Table 1. Proteins used.

Rabbit	Protein A*			Protein B†			Protein C‡	
	Protein	Amount (mg)	Volume (ml)	Protein	Amount (mg)	Volume (ml)	Protein	Amount (mg)
845	Human serum albumin	2500	10.0	Radioiodinated rabbit gamma globulin	93.2	4.0	Bovine gamma globulin	119
846	Human serum albumin	2500	10.0	Radioiodinated rabbit gamma globulin	93.2	4.0	Bovine gamma globulin	119
847	Radioiodinated rabbit gamma globulin	233	10.0	Human serum albumin	1250	5.0	Bovine gamma globulin	119
849	Bovine gamma globulin	1000	10.0	Human serum albumin	1250	5.0	Radioiodinated rabbit gamma globulin	46.6
852	Bovine gamma globulin	1000	10.0	Human serum albumin	1250	5.0	Radioiodinated rabbit gamma globulin	46.6
817	Human serum albumin	1250	5.0	Bovine serum albumin	300	2.0	Bovine gamma globulin	11.0

* Injected intravenously 48 hr before injection of protein B.

† Animals sacrificed 15 min after intravenous injection of protein B.

‡ Added to muscle homogenates.

Table 2. Concentration of homologous and heterologous plasma proteins in the interstitial fluid of rabbit muscle.

Rabbit	Muscle wet wt. (g)	Serum concentrations		Volume of distribution of protein C* (ml)	Total found in muscle sample		Amount of serum in muscle sample† (ml)	Amount A in muscle in excess of contribution by serum‡ (mg)	Interstitial concentration of A§ (mg/ml)	Serum conc. A interstitial
		Prot. A (mg/ml)	Prot. B (mg/ml)		Prot. A (mg)	Prot. B (mg)				
845	26.3	6.29	0.608	73.4	10.86	0.276	0.454	8.00	2.25	2.80
846	36.8	7.30	.696	79.3	15.22	.178	.256	13.46	2.75	2.67
847	27.0	0.312	10.39	95.2	0.454	3.90	.375	0.337	0.0924	3.38
849	21.3	2.74	10.90	90.0	3.15	2.16	.193	2.62	.911	2.99
852	32.7	2.38	8.70	80.0	5.76	4.24	.487	4.60	1.04	2.28
817a	18.4	3.44	2.54	93.6	3.18	0.467	.184	2.55	1.03	3.34
817b	17.9	3.44	2.54	65.0	3.25	.660	.260	2.36	0.976	3.52
817c	22.0	3.44	2.54	93.6	3.09	.373	.147	2.58	.868	3.97

* Eq. 1. † Eq. 3. ‡ Eq. 2. § Assuming an interstitial fluid of 13.5 percent; Eq. 6.

Finally,

$$A_i = \frac{A_s}{FW} \times 100, \quad (6)$$

where A_i is the concentration of A in the interstitial fluid, F is the percentage of free interstitial fluid in muscle, and W is the wet weight of the muscle sample.

The proteins used in this study for each rabbit are listed in Table 1. It is to be noted that (i) the proteins were used in a variety of combinations in an attempt to eliminate possible errors resulting from a peculiarity in the properties of one or more of the proteins used, such as selective adsorption to tissue elements; (ii) both radioactivity and immunochemical measurements were employed in combination, and (iii) both heterologous and homologous plasma proteins were used in various combinations. The immunochemical (10) and radioiodine (11) procedures have been described in detail elsewhere. All native proteins studied were estimated immunochemically.

Results. The results are shown in Table 2. It will be noted that the average residual serum in the muscle samples was about 1.5 percent of the muscle wet weight, and the average residual whole blood, therefore, was about 2.5 percent. On the basis of chloride analyses, Harrison *et al.* (12) found that the volume of extracellular fluid in muscle obtained from exsanguinated rabbits similar to those studied in this report was 16 percent of the wet tissue weight. Correcting for the average residual whole blood, the average interstitial fluid volume of the muscle samples in Table 2 was about 13.5 percent of the wet weight of the sample (13). For the proteins studied, an average ratio of 3 : 1 was found between the concentration of a plasma protein in serum and its concentration in interstitial fluid. The values obtained for the amount of a given plasma protein present extravascularly after 48 hr equilibration in the rabbit compare reason-

ably well, as can be seen in Table 3, with those obtained from calculations based on the premise that, in the steady state, roughly as much plasma protein is present outside the blood vessels as is present within the blood vessels.

The ratios of serum protein to interstitial plasma protein, given in Table 2, agree with those given by Weech *et al.* (14) for the ratios of serum protein to lymph protein and would appear to substantiate the opinion that the lymph protein concentrations are representative of the protein concentrations of the interstitial fluid (15). The presence of such relatively large quantities of plasma protein in the fluid outside the capillaries does not mitigate against Starling's hypothesis of the capillary (16) but instead simply serves to modify quantitatively the balance of forces influencing the transfer of water and solutes across the capillary wall.

Table 3. Comparison of amount of interstitial plasma protein found with that expected.

Rabbit	Amount plasma protein in interstitial fluid	
	Expected* (mg)	Found (mg)
845	8.3	8.00
846	13.4	13.46
847	0.42	0.337
849	2.9	2.62
852	3.9	4.60
817a	3.2	2.55
817b	3.1	2.36
817c	3.8	2.58

* Plasma volume of muscle sample assumed to be 5 percent. On the assumption that $A_i = A_s$, the expected amount = 5 percent wet weight of sample \times serum concentration.

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Mass Separation of Reticuloendothelial and Parenchymal Cells of Rat's Liver

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Recent studies (1, 2) have emphasized the importance of the hepatic reticuloendothelial (RE) system in the disposition of exogenously derived cholesterol. Consequently it appeared necessary to study these cells more closely than has been done.

A few years ago, Rous and Beard (3) were able to collect some RE cells by perfusing the liver of an animal injected with iron. The iron-containing RE cells present in the perfusate were isolated by means of an electromagnet. More recently, Anderson (4) described a method by which the total liver could be reduced to a suspension of its constituent cells. We believed these two different procedures, if combined, might offer a method for the separation and collection of relatively pure, viable hepatic parenchymal and RE cells in quantities sufficient so that the functions of each could be studied independently of the other. The method (5) described here achieved this separation.

The livers of rats that had been injected intravenously with 1 ml of a suspension of 15 percent pulverized carbonyl iron and 5 percent starch in saline on 3 successive days were perfused forward through the aorta and backward via the superior vena cava with isotonic calcium-sequestering fluid (1 part 0.11M versene, pH 7.4 to 9 parts Locke).

The entire liver was then removed and forced through a tissue press (garlic press) into a sufficient volume of fresh perfusion fluid to make a 3 to 4 percent suspension, stirred gently for about 10 min, and

then poured through a 10 XX silk screen. Approximately 90 percent of the screen filtrate consists of intact liver cells.

The cell suspension was poured into conical siliconed centrifuge tubes and centrifuged at 45 g for 2 min. An upper, relatively clear supernatant layer (containing broken cells, vascular elements, and some of the non-iron-containing reticuloocytes) was drawn off and discarded. The remaining two layers, the relatively cream-colored upper layer containing mostly hepatic parenchymal cells and the lower grey-black sediment containing RE cells preponderantly, were removed separately, resuspended in the perfusion fluid, centrifuged and separated as before, adding each layer to its respective counterpart obtained after the first centrifugation. This centrifuging washing procedure was repeated 3 times in all.

In order to obtain a pure collection of RE cells, the combined lower layers were suspended in 20 vol of a 4-percent solution of starch in isotonic saline containing 1 ml of 0.3 percent digitonin and 2 ml of Kreb's isotonic phosphate buffer per 100 ml. This suspension, although still containing some parenchymal cells, consists mainly of iron-containing RE cells.

The cell suspension was poured into a conical tube held upright in the field of a large eye magnet. The tube was rotated while being raised so that the magnetized cells described a helix as they were brought from the mouth to the apex of the tube. The fluid was then removed and resubmitted to the magnet as before. The procedure was repeated once more. All the sediments of iron-containing cells were combined, resuspended in the starch solution, and again brought to the bottom of the tube by the magnet. This resulted in a collection of RE cells of high purity (Fig. 1). In



Fig. 1. Magnetized hepatic RE cells, unstained ($\times 800$).

order to segregate hepatic parenchymal cells, the upper sedimentary layers obtained from the initial centrifugal process were suspended in perfusate and submitted to the magnet. The few iron-containing RE cells were quickly moved to the bottom of this non-viscous medium, and the upper layer on removal contained a morphologically homogeneous suspension of parenchymal cells (Fig. 2).

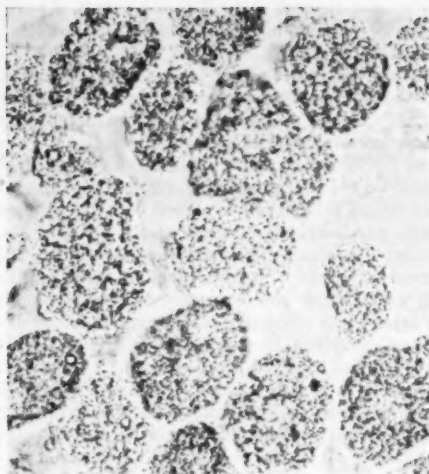


Fig. 2. Hepatic parenchymal cells from the same liver after separation from the RE cells, unstained ($\times 800$).

The afore-described procedure does not appear to destroy structural integrity of the cells, because neither cholesterol or biuret protein could be detected in the suspension fluid even after 4 hr of storage. Furthermore, the washed cells were observed, after the addition of ATP, to reduce triphenyl tetrazolium chloride at a normal rate.

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Effect of Maleic Hydrazide on the Respiration of Mature Onion Bulbs

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In a previous paper (1) the effects of aqueous sprays of maleic hydrazide on young, rapidly growing onion plants were presented. Results of enzyme assays indicated that maleic hydrazide reduced the dehydrogenase activity of the treated plants. The present paper (2) reports the respiratory effects of maleic hydrazide on stored mature onion bulbs harvested from plants previously treated with foliar applications of the hydrazide.

Sweet Spanish onions, Utah strain, were grown from seed and 14 wk after planting were treated with

foliar sprays containing 500, 1000, 2000, 3000, and 4000 ppm of maleic hydrazide applied in the form of the diethanolamine salt at the rate of 0.16, 0.32, 0.64, 0.96, and 1.28 lb/acre of the free hydrazide. The mature bulbs were harvested 17 days after the hydrazide treatment, cured at room temperature for 2 wk, and placed in storage at 1°C for 23 wk.

After the storage period, it was observed that treatments of 3000 and 4000 ppm of maleic hydrazide greatly inhibited sprouting, whereas nontreated bulbs and bulbs treated with low concentrations of the hydrazide exhibited considerable sprouting.

Dehydrogenase activity and respiration as measured in a Warburg respirometer were determined on suspensions of onion bulbs minced in equal weights of phosphate buffer at pH 7.4. An anaerobic technique employing p,p'-diphenylenebis-2-(3,5-diphenyltetrazolium chloride), DBDTC, was used for the estimation of dehydrogenase activity (3). The colored reduction product was extracted with benzene and the optical density of the solution was read at 520 m μ . Oxygen absorption and carbon dioxide production were determined on the minced suspensions for 2 hr at 37.5°C .

At the end of the 23-wk storage period the effect of maleic hydrazide applications was evident, as indicated by the dehydrogenase activity and the respiration of the stored bulbs. The results of four determinations (Fig. 1) indicate that maleic hydrazide applications are stimulatory to respiration at low concentrations and inhibitory at high concentrations. An increase of the dehydrogenase activity and oxygen absorption could be obtained by the addition of succinate to those minces prepared from plants receiving low concentrations of the hydrazide. No stimulation of the enzyme system could be obtained by the

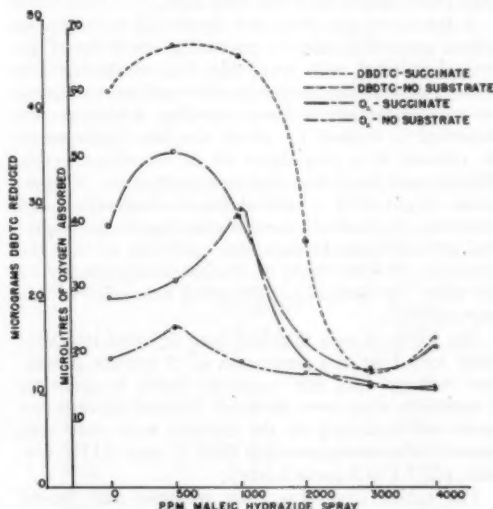


Fig. 1. Effect of maleic hydrazide on dehydrogenase activity and on oxygen absorption, as determined on 1 ml of minced onion tissue containing 58 mg of dry matter.

Table 1. Correlation coefficients between dehydrogenase activity (DBDTC reduced) and respiration of onions as affected by maleic hydrazide treatment.

	DBDTC reduced as compared with	
	O ₂ absorbed	CO ₂ evolved
Succinate added	+ 0.908*	+ 0.753
No substrate added	+ 0.929†	+ 0.938†

* Significant at the 5 percent level.

† Significant at the 1 percent level.

addition of the substrate to preparations made from material treated with high concentrations of maleic hydrazide. Succinic dehydrogenase appears to be markedly inhibited in material treated with high concentrations of maleic hydrazide. Examination of the data indicated a positive correlation between respiratory activity as measured by DBDTC reduction and

by oxygen absorption. Correlation coefficients are given in Table 1 and suggest that the same phenomena are being measured by both methods.

Growth inhibition from applications of moderate concentrations of maleic hydrazide usually takes place for a limited time, the duration being dependent on the concentration of the applied material (4). The ability of the treated plant to recover its normal growth after an initial inhibition suggests that maleic hydrazide is converted to noninhibitory compounds. At high concentrations of the hydrazide, the conversion may be so slow that concentrations inhibitory to respiration remain after long periods.

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4 June 1954.

Communications

Scientists and the McCarran Act

In the 19 June 1954 issue of the *Saturday Evening Post* there appeared an editorial under the title, "McCarran Act will bar no genuine visiting scientists." The editor referred to a recent lecture at Philadelphia, in which I described the difficulties that the U.S. national committees of various scientific unions face when they consider invitations to their unions for meetings in this country. The article implies that I am one of those who "are moving heaven and earth to undermine our immigration policy," and that the purpose of my lecture was "to scrap the McCarran Act," a purpose that is also shared by the World Council of Churches. The editor continues by asserting that under the present interpretation of the immigration act no genuine visiting scientist will be barred unless "he turns out to be a really bad egg."

On 28 June I wrote to the editor of the *Post*, but, after having at first offered to print my letter, Frederic Nelson, associate editor, has now informed me that "the editor who runs our correspondence column feels that we have printed all the letters he thinks we should on the McCarran Act editorial," and that while he himself is sorry about this decision he doubts "that many readers would have reached the conclusion that you should be associated with those who are attempting to change the national policy on immigration." My letter of 28 June was as follows:

I must take exception to some statements made in your editorial of 19 June concerning the McCarran Act and its effect upon the admission "to our shores" of foreign scientists—those who are not "really bad eggs." You are wrong in associating me with "groups who are moving heaven and earth to undermine our immigration policy." As an astronomer, I know full

well that the laws of Newton and Kepler will forever prevent me or anyone else from moving either the earth or the heavens. The heavenly bodies are one of my main interests in life, but my "heavenly" interests do not extend as far as the World Council of Churches, and I do not carry the ball for them.

But regarding our man-made laws, there is one aspect about which I am concerned. Do you really think, Mr. Editor, that there is nothing wrong with our present visa policy as it affects the scientists? I do not advocate, and I have never done so, that we "scrap the McCarran Act."

I am a Russian-born naturalized citizen of the United States to whom America has been good, and all my actions since I came "to these shores" in 1921 and all my public statements have been intended to help in the protection of the freedom and the greatness of our country. I warned against the dangers of Russian communism when it was quite unpopular for anyone to do so. And I am not likely to forget the wounds—physical and spiritual—that I suffered as a young officer in the desperate struggle against the Reds when they seized power in Russia. But, as a scientist, it is also my duty to bring to the attention of the people that, for our own protection, (i) we need the knowledge of foreign scientists, and (ii) we must seek and keep their friendship. Do you remember the words of President Truman on 8 Aug. 1945, when he announced the dropping of the first atom bomb over Hiroshima: "Sixteen hours ago an American airplane dropped one bomb on Hiroshima. . . . It is an atomic bomb. It is a harnessing of the basic power of the universe. The force from which the sun draws its powers has been loosed against those who brought war to the Far East." The sun was our clue to the solution of the problem of atomic energy, and all our great physicists—Bethe, Teller, and Oppenheimer too—knew that atomic power on a tremendous scale was possible, because astronomers had told them

that this very power was what made the sun and the stars shine. How did the astronomers know this? About equally, I should say, from the work of the American astronomers, under the banner of our own great Henry Norris Russell of Princeton University, and from that of western European scientists, under the unchallenged leadership of the late Arthur Stanley Eddington of Cambridge University, England. Eddington is dead, but his former close associate, the brilliant Nobel prize winner in physics, P. A. M. Dirac, was recently refused entry into the United States. I do not believe that even under your interpretation he could be described as a "really bad egg." His knowledge, and that of others like him, is tremendously important to us. In any case, we should not be too reluctant to add a small dose of that kind of egg to our domestic diet.

I have been given the honor, and at the same time the responsibility, of serving as the president of the International Astronomical Union, an organization of scientists representing 35 different countries of the world. It was founded in 1919, largely through the efforts of the late George Ellery Hale, the man who built for America the 40-in. refracting telescope of the Yerkes Observatory and the 100-in. reflector at Mount Wilson, and who began the construction of

the giant 200-in. telescope on Palomar Mountain. We are very anxious that our Union hold one of its next meetings in this country. But, rightly or wrongly, many foreign astronomers, some of whom have previously been refused entry into the United States, are afraid to apply. The refusal of a visa labels them as "red" or "pink" in their own countries.

This is not a partisan matter, and I should regret it if emotional issues, either for or against my proposal, should arise from it. My proposal is a simple one: that the Attorney General be requested to exercise the power granted to him under the present law to admit, for 2 or 3 weeks, all qualified astronomers to attend a congress to be held under the great domes of Palomar Mountain, Mount Wilson, and Lick Observatories. America is proud of these monuments of achievement by some of its greatest astronomers. The work done with these telescopes is non-secret, basic research. The opportunity is ours to demonstrate to the world the strength of our science. We need your help and that of our Government to accomplish this.

Berkeley Astronomical Department,
University of California, Berkeley

OTTO STRUVE

2 August 1954.

A Method for Controlling Pain of the Face and Jaws Caused by Tic Douloureux

A new method for controlling the chronic recurring face pain of tic douloureux that we have developed entails the partial or complete destruction of the nerve cells of the Gasserian ganglion by injection of boiling water into this sensitive nerve center from which the pain originates.

The injection is performed in the radiographic room under light pentothal anesthesia with the aid of a Franklin x-ray head stand. By repeated roentgenograms, the foramen ovale at the base of the skull is visualized, and a 3 $\frac{3}{4}$ -in. spinal needle is inserted through it into the ganglion. The needle puncture is made through the skin of the cheek at a point 3 cm below the malar bone and between the ramus of the mandible and maxilla. At some point between 12 and 17 mm from the foraminal edge, blood tinged cerebrospinal fluid is obtained by jugular compression or syringe aspiration, which indicates that the needle has pierced the arachnoid reflection surrounding the ganglion and sensory root of the fifth cranial nerve and that it has been properly placed. Then 1 ml of boiling distilled water is injected. Under light anesthesia, there can be demonstrated by pinprick an area of diminished sensation on the face corresponding to the well-known anatomic distribution of the ganglion. Additional 1-ml injections of water produce a more profound loss of face sensation. It is possible to stop the pain without producing a major sensory loss by injection of smaller quantities of water.

Any analgesic effect produced is believed to be permanent, which is desirable since tic douloureux is incurable except by a major intracranial operation or destruction of the ganglion by alcohol. It is improbable that damage to the brain or other cranial nerves will result if no more than 1 ml of water is injected at any one time, since the water temperature is immediately lowered to a safe level the instant it is diluted by the intracranial cerebrospinal fluid.

This method has always produced a paralysis of the muscles of mastication, which may be detected on careful examination of the masseter and temporal muscles. It is believed that this is temporary and that the motor branch will regenerate.

The method makes possible the relief from the lifelong pain of tic douloureux without the hazards of a major operation or of alcohol injection, as has been necessary in the past. Since most of those suffering from this disorder are elderly persons in poor physical condition for an operation, the procedure can be used without the risks inherent in the other standard procedures required for permanent relief.

Fourteen cases of tic douloureux have been successfully relieved of their pain by this method, since the first case was so treated on 30 Oct. 1953, without a major complication. One case of cancer of the jaw has been relieved of pain by this procedure.

RUDOLPH JAEGER

Department of Neurosurgery,
Jefferson Medical College,
Philadelphia, Pennsylvania

18 May 1954.

Meetings & Conferences

October

- 18-21. Mental Hospital Inst., 6th, Minneapolis, Minn. (W. Malamud, 80 E. Concord St., Boston 18.)
- 18-22. American Soc. of Civil Engineers, New York City. (W. M. Carey, 33 W. 39 St., New York 18.)
- 19. American Soc. of Safety Engineers, Chicago. (J. B. Johnson, 425 N. Michigan Ave., Chicago 11.)
- 21-22. National Noise Abatement Symposium, 5th annual, Chicago. (S. M. Potter, Illinois Inst. of Technology, Chicago 16.)
- 21-23. International Assoc. of Milk and Food Sanitarians, Atlantic City, N.J. (H. L. Thommasson, IAMFS, Box 437, Shelbyville, Ind.)
- 21-23. International Symposium on the Dynamics of Virus Infections, Detroit. (Henry Ford Hospital, 2799 W. Grand Blvd., Detroit 2.)
- 21-24. American Dietetic Assoc., annual Philadelphia. (E. A. Atkinson, 620 N. Michigan Ave., Chicago 11.)
- 22. Symposium on the Nutritional Aspects of Blood Formation, Cincinnati, Ohio. (National Vitamin Foundation, 15 E. 53 St., New York 22.)
- 22-23. Canadian Physiological Soc., Toronto, Ont., Canada. (J. M. R. Beveridge, Dept. of Biochemistry, Queen's University, Kingston, Ont.)
- 22-26. Symposium on Wind and Solar Energy, New Delhi, India. (UNESCO, 19 Ave. Kléber, Paris 16.)
- 24-27. Soc. of American Foresters, Milwaukee. (H. Clepper, 425 Mills Bldg., Washington 6, D.C.)
- 25-27. Assoc. of American Medical Colleges, Bedford Springs, Pa. (AAMC, 5 S. Wabash Ave., Chicago 3.)
- 25-30. International Cong. of Odontology, 1st, São Paulo, Brazil. (F. Degni, Rua Marconi 131, São Paulo.)
- 26. Assoc. of Consulting Chemists and Chemical Engineers, annual, New York City. (A. B. Bowers, 50 E. 41 St., New York 17.)
- 27-28. Conf. on Plastics in Building, Washington, D.C. (Building Research Inst., 2101 Constitution Ave., Washington 25.)
- 27-29. International Symposium on the Hypophyseal Growth Hormone, Its Nature and Actions, Detroit, Mich. (R. W. Smith, Henry Ford Hospital, Detroit 2.)
- 28-30. American Soc. for Aesthetics, Bloomington, Ind. (R. R. Patrick, Cleveland Museum of Art, Cleveland 6, Ohio.)
- 28-30. International Symposium on Temperature, Washington, D.C. (W. Waterfall, 57 E. 55 St., New York 22.)
- 31-1. American Soc. for the Study of Arteriosclerosis, annual, Chicago. (A. C. Corcoran, Cleveland Clinic, Cleveland 6, Ohio.)

November

- 1-5. Entomological Societies of Canada and Ontario, annual, Sault Ste. Marie, Canada. (R. H. Wigmore, Science Service Bldg., Ottawa.)
- 1-3. Geological Soc. of America, annual, Los Angeles, Calif. (H. R. Aldrich, 419 W. 117 St., New York 27.)
- 1-5. Paleontological Soc., annual, Los Angeles, Calif. (K. E. Caster, Dept. of Geology, Univ. of Cincinnati, Cincinnati 21, O.)
- 1-5. National Metal Cong., Chicago, Ill. (C. L. Wells, 7301 Euclid Ave., Cleveland, O.)
- 3-5. American Crystallographic Assoc., and 12th annual Pittsburgh Diffraction Cong., Pittsburgh, Pa. (P. K. Koh, Allegheny Ludlum Research Laboratories, Alabama Ave., Brackenridge, Pa.)

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Meetings & Conferences

November, *contd.*

- 3-5. Soc. of Rheology, Washington, D.C. (W. R. Willets, Titanium Pigment Corp., 99 Hudson St., New York 13.)
- 3-6. American Soc. of Parasitologists, Memphis, Tenn. (A. C. Walton, Dept. of Biology, Knox College, Galesburg, Ill.)
- 3-6. American Soc. of Tropical Medicine and Hygiene, Memphis, Tenn. (J. E. Larsh, Jr., School of Public Health, Univ. of North Carolina, Chapel Hill.)
- 4-5. Hawaiian Acad. of Science, Honolulu, Hawaii. (D. C. Cox, Experiment Station, HSPA, Honolulu 14.)
- 4-6. American Acad. of Tropical Medicine, Memphis, Tenn. (E. H. Hinman, Univ. of Puerto Rico School of Medicine, San Juan 22.)
6. Committee for the Scientific Study of Religion, fall, Cambridge, Mass. (R. V. McCann, 48 Mt. Auburn St., Cambridge.)
7. American College of Dentists, Miami, Fla. (O. W. Brandhorst, 4221 Lindell Blvd., St. Louis, Mo.)
- 7-12. International Cong. of Military Medicine and Pharmacy, Luxemburg, Luxembourg. (A. R. Vernengo, Pozos 2045, Buenos Aires, Argentina.)
- 8-11. American Dental Assoc., annual, Miami, Fla. (H. Hillenbrand, 222 E. Superior St., Chicago 11, Ill.)
- 8-11. American Petroleum Inst., 34th annual, Chicago, Ill. (API, 50 W. 50 St., New York 20.)
- 8-11. Southern Soc. of Cancer Cytology, annual, St. Louis, Mo. (J. E. Ayre, 1155 N. W. 14 St., Miami, Fla.)
- 8-12. American Soc. of Agronomy, annual, St. Paul, Minn. (L. G. Monthey, 2702 Monroe St., Madison 5, Wis.)
- 8-12. Soil Conservation Soc. of America, St. Paul, Minn. (H. W. Pritchard, 1016 Paramount Bldg., Des Moines, Iowa.)
- 10-11. Conf. on Electrical Techniques in Medicine and Biology, Chicago, Ill. (E. D. Trout 4855 Electric Ave., Milwaukee, Wis.)
- 11-12. Corrosion Cong., Frankfurt, Germany. (DE-CHEMA, Frankfurt a.M., W. 13.)
- 12-13. Inter-Society Cytology Council, Boston, Mass. (P. F. Fletcher, 634 N. Grand Blvd., St. Louis 3, Mo.)
- 12-Dec. 11. United Nations Educational, Scientific, and Cultural Organization, Montevideo, Uruguay. (UNESCO, 19 Ave. Kléber, Paris 16.)
- 15-17. National Conf. on Standards, 5th, New York City. (D. E. Denton, 70 E. 45 St., New York 17.)
- 17-19. American Meteorological Soc., Miami Beach, Fla. (K. C. Spengler, 3 Joy St., Boston 8, Mass.)
- 18-20. Acoustical Soc. of America, semiannual, Austin, Tex. (W. Waterfall, 57 E. 55 St., New York 22.)
- 18-20. Symposium on Precision Electrical Measurements, Teddington, Eng. (Director, National Physical Laboratory, Teddington, Middlesex, Eng.)
- 19-20. International Cong. of Civil Engineers, 2nd, Caracas, Venezuela. (L. B. Diaz, Av. Principal de los Caobos, Apartado 2006, Caracas.)
- 26-27. American Physical Soc., Chicago, Ill. (K. K. Darrow, Columbia Univ., New York 27.)
- 26-27. American Soc. of Animal Production, Chicago, Ill. (W. M. Beeson, Dept. of Animal Husbandry, Purdue Univ., Lafayette, Ind.)
- 26-27. Tennessee Acad. of Science, Nashville, Tenn. (I. H. Tipton, Physics Dept., Univ. of Tennessee, Knoxville.)

Meetings & Conferences

November, *contd.*

- 28-1. American Soc. of Refrigerating Engineers, Philadelphia, Pa. (J. I. Szabo, 40 W. 40 St., New York 18.)
 28-3. American Soc. of Mechanical Engineers, annual, New York City. (O. B. Schier, II, 29 W. 39 St., New York 18.)
 29-1. Assoc. of Military Surgeons, Washington, D.C. (R. R. Sayers, Armed Forces Inst. of Pathology, Washington 25.)
 29-2. American Medical Assoc., clinical, Miami, Fla. (G. F. Lull, 535 Dearborn St., Chicago 10, Ill.)

December

- 1-3. American Rocket Soc., New York, N.Y. (ARS, 33 W. 39 St., New York 18.)
 1-7. International Cong. on Medicinal and Similar Plants, São Paulo, Brazil. (P. Artigas, Rua Tres Rios 363, São Paulo.)
 1-8. Pan American Pharmaceutical and Biochemical Cong., 3rd, São Paulo, Brazil. (C. Fontoura, Rua Caetano Pinto 129, São Paulo.)
 3-4. Oklahoma Acad. of Science, Tulsa, Okla. (R. E. Olson, Dept. of Geography, Univ. of Oklahoma, Norman.)
 3-5. American Psychoanalytic Assoc., New York, N.Y. (R. L. Frank, 745 5 Ave., New York 22.)
 4. American Alpine Club, Philadelphia, Pa. (J. C. Oberlin, 909 Leader Bldg., Cleveland 14, Ohio.)
 5. American Acad. of Dental Medicine, 9th mid-annual, New York, N.Y. (W. M. Greenhut, 124 E. 84 St., New York 28.)
 5-8. American Soc. of Agricultural Engineers, winter, Chicago, Ill. (F. B. Lanham, ASAE, St. Joseph, Mich.)
 5-10. Radiological Soc. of North America, annual, New York, N.Y. (D. S. Childs, 713 E. Genesee St., Syracuse 2, N.Y.)
 6-9. Entomological Soc. of America, Houston, Tex. (A. B. Gurney, 1530 P St., NW, Washington 5.)
 8-10. Eastern Joint Computer Conf., 4th annual, Philadelphia, Pa. (EJCC, P.O. Box 7825, Philadelphia 1.)
 9-11. Texas Acad. of Science, annual, San Antonio, Tex. (G. H. Baird, P.O. Box 228, Huntsville.)
 10-12. Florida Acad. of Science, Tallahassee, Fla. (R. A. Edwards, Dept. of Geology, Univ. of Florida, Gainesville.)
 11-14. American Acad. of Optometry, annual, Toronto, Canada. (C. C. Koch, 1502 Foshay Tower, Minneapolis 2.)
 11-22. World Forestry Cong., 4th, Dehra Dun, India. (T. Street, Foreign Agricultural Service, U.S. Department of Agriculture, Washington 25.)
 12-15. American Inst. of Chemical Engineers, annual, New York, N.Y. (AIChE, 120 E. 41 St., New York 17.)
 26-28. American Statistical Assoc., Berkeley, Calif. (S. Weiss, 1108 16 St., NW, Washington 6.)
 26-29. National Science Teachers Assoc., Berkeley, Calif. (R. H. Carleton, 1201 16 St., NW, Washington 6.)
 26-30. Inst. of Mathematical Statistics, Berkeley, Calif. (K. J. Arnold, Dept. of Mathematics, Michigan State College, E. Lansing.)
 26-31. AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, annual, Berkeley, Calif. (R. L. Taylor, 1515 Massachusetts Ave., NW, Washington 5.)
 26-31. American Nature Study Soc., Berkeley, Calif. (H. B. Ross, State Teachers College, Fitchburg, Mass.)

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Meetings & Conferences

December, *contd.*

27. Metric Assoc., Washington, D.C. (V. G. Shinkle, 1916 Eye St., NW, Washington 6.)
- 27-28. American Folklore Soc., New York, N.Y. (M. Leach, Bennett Hall, Univ. of Pennsylvania, Philadelphia 4.)
- 27-28. Ecological Soc. of America, Berkeley, Calif. (J. F. Reed, Dept. of Botany, Univ. of Wyoming, Laramie.)
- 27-29. American Mathematical Soc., annual, Pittsburgh, Pa. (E. G. Begle, AMS, Yale University, New Haven, Conn.)
- 27-29. Arctic Inst. of North America, Berkeley, Calif. (R. C. Wallace, 4 Centre St., Kingston, Ont., Canada.)
- 27-29. Astronomical Soc. of the Pacific, Berkeley, Calif. (S. Einarsson, Leuschner Observatory, Univ. of California, Berkeley 4.)
- 27-29. International Conf. on Animal Venoms, Berkeley, Calif. (N. Porges, Eastern Regional Research Laboratory at Wyndmoor, Philadelphia, Pa.)
- 27-29. Western Soc. of Naturalists, Berkeley, Calif. (J. L. Mohr, Univ. of Southern California, Los Angeles 7.)
- 27-30. Berkeley Symposium on Mathematical Statistics and Probability, 3rd, Berkeley, Calif. (J. Neyman, Dept. of Mathematics, Univ. of California, Berkeley 4.)
- 27-30. Econometric Soc., Detroit, Mich. (R. L. Cardwell, Cowles Commission, Univ. of Chicago, Chicago 37.)
- 27-30. National Assoc. of Biology Teachers, Berkeley, Calif. (P. Webster, Bryan City High School, Bryan, Ohio.)
- 27-30. Soc. of Systematic Zoology, Berkeley, Calif. (R. E. Blackwelder, U.S. National Museum, Washington 25.)
- 28-29. Linguistic Soc. of America, Detroit, Mich. (A. A. Hill, 1719 Massachusetts Ave., NW, Washington 6.)
- 28-29. Meteorological Soc., Berkeley, Calif. (J. A. Russell, Univ. of Southern California, Los Angeles 7.)
- 28-29. Northwest Scientific Assoc., Missoula, Mont. (F. J. Schadegg, Eastern Washington College of Education, Cheney, Wash.)
- 28-30. American Economic Assoc., Detroit, Mich. (J. W. Bell, Dept. of Economics, Northwestern Univ., Evanston, Ill.)
- 28-30. American Meteorological Soc., Berkeley, Calif. (K. C. Spengler, 3 Joy St., Boston 8, Mass.)
- 28-30. American Physical Soc., Berkeley, Calif. (J. Kaplan, Dept. of Physics, Univ. of California, Los Angeles 24.)
- 28-30. American Soc. of Limnology and Oceanography, Berkeley, Calif. (B. H. K. Ketchum, Woods Hole Oceanographic Institution, Woods Hole, Mass.)
- 28-30. American Soc. of Zoologists, Chapel Hill, N.C. (R. T. Kempton, Vassar College, Poughkeepsie, N.Y.)
- 28-30. Archaeological Inst. of America, annual, Boston, Mass. (C. G. Yavis, Andover Hall, Francis Ave., Cambridge 38, Mass.)
- 28-30. Gerontological Soc., annual, Gainesville, Fla. (N. W. Shock, Baltimore City Hospitals, Baltimore 24, Md.)
29. Assoc. for Symbolic Logic, Pittsburgh, Pa. (J. Barlaz, Rutgers Univ., New Brunswick, N.J.)
- 29-30. History of Science Soc., New York, N.Y. (M. Boas, Brandeis Univ., Waltham, Mass.)
30. Mathematical Assoc. of America, Pittsburgh, Pa. (H. M. Gehman, Univ. of Buffalo, Buffalo 14, N.Y.)
30. Soc. of General Physiologists, Berkeley, Calif. (J. B. Buck, National Institutes of Health, Bethesda 14, Md.)

Miscellaneous Publications

International Statistical Conferences, December 1951, India. Bull., vol. 33, pt. 2. *Mathematical Statistics and Biometry*, 404 pp., Illus., \$7.50; pt. 3, *Income and Wealth, Econometrics and Economic Statistics*, 350 pp., Illus., \$5.25; pt. 4, *Demography and Labour Statistics*, 280 pp., Illus., \$5. International Statistical Institute, Calcutta.

National Vitamin Foundation Incorporated 1953 Annual Report of the Scientific Director. The Foundation, New York 22, 1954. 87 pp.

Laboratory Techniques in Rabies. Monogr. Ser., No. 23. World Health Organization, Geneva, 1954 (Order from Columbia Univ. Press, New York 27). 150 pp. Illus. + plate. \$3.

People to People Diplomacy. International Information and Cultural Ser., 36. Dept. of State, Washington 25, 1954 (Order from Supt. of Documents, GPO, Washington 25). 29 pp. Illus. 20¢.

Indo-Pacific Fisheries Council Proceedings. 5th meeting, 22 Jan.-5 Feb. 1954, Bangkok, Thailand. Sec. 1. IPFC Secretariat, Food and Agriculture Organization of the United Nations, Bangkok, 1954. 111 pp. \$1.

Proceedings of the United Nations Scientific Conference on the Conservation and Utilization of Resources. 17 Aug.-6 Sept. 1949, Lake Success, N.Y. vol. 8, Index. Dept. of Economic Affairs, United Nations, New York, 1953 (Order from Columbia Univ. Press, New York 27). 134 pp. \$1.50.

Probleme der Krebsforschung und Krebsbekämpfung. Abhandlungen der Deutschen Akademie der Wissenschaften zu Berlin, Klasse für Medizinische Wissenschaften, Jahrgang 1953, No. 1. Akademie-Verlag, Berlin, 1954. 168 pp. Illus. DM. 12.

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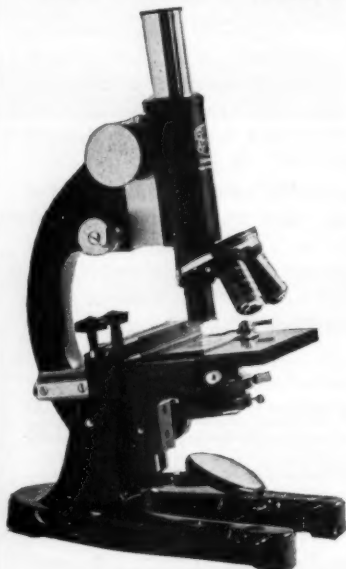
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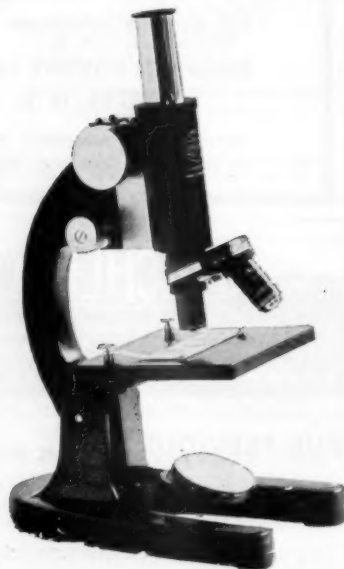
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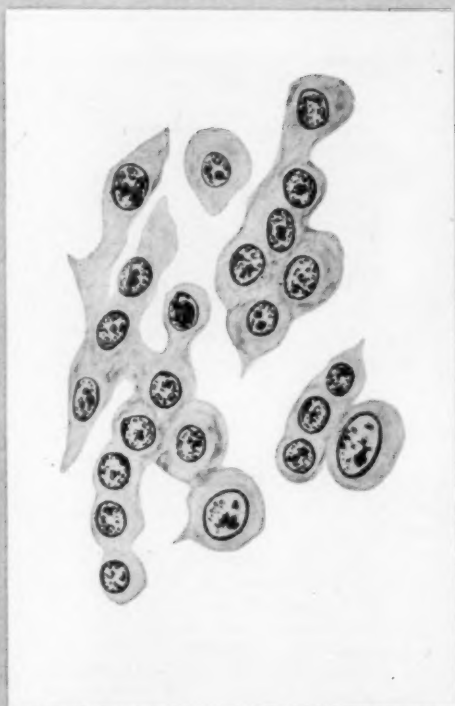
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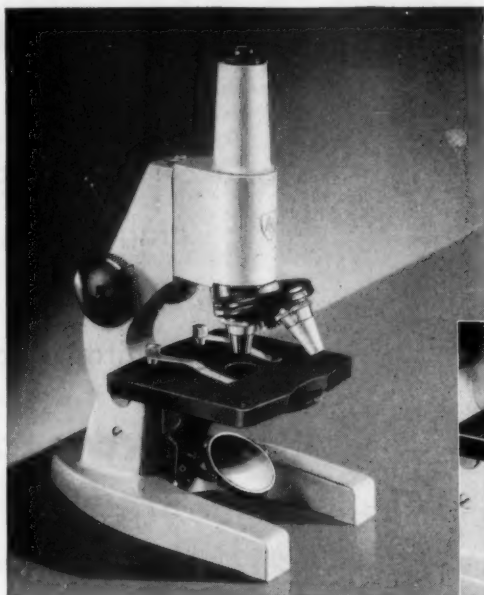
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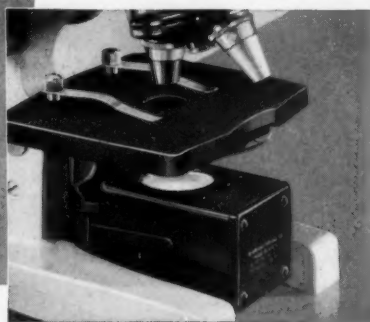


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